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Molecular characterization of patients sensitized to aeroallergens with rhinitis and asthma

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MOLECULAR CHARACTERIZATION OF PATIENTS SENSITIZED TO AEROALLERGENS WITH RHINITIS AND ASTHMA

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Abstract

Background: Sensitization to aeroallergens is important in patients with allergic rhinitis and asthma. *Aim:* investigate the prevalence of specific IgE sensitization.

Methods: Frequency and rates of positivity of specific IgE to aeroallergens were analysed in 993 sensitized patients with asthma and/or rhinitis. The molecular sensitization profile to Der p1, Der p2, Der p10, Phl p1, Phl p5, Phl p7, Phl p12, Ole e1, Ole e7, Ole e9 and Par j2 was studied in 303 patients.

Results: From 993 patients (63.9% had rhinitis, 36.1% had asthma), specifc IgE sensitization rates were 78% to mites, 44% to grass pollens, 14% to olive, 9% to *Parietaria* and 3% to *Alternaria*. Asthmatic patients had higher sensitization to house dust mites (p=0.001) and patients with rhinitis to grass pollens (p=0.044). Positivity to Der p1 was 54.7%, to Der p2 66.7%, to Der p10 14.7%, to Phl p1 72.2%, to Phl p5b 38.9%, to Phl p7 13.0% and to Phl p12 21.1%. Sensitization exclusively to species allergens Phl p1 and/or Phl p5 and/or Ole e1 was 38.2%.

Conclusions: Phl p1 was the main molecular aeroallergen and Der p2 had a higher positivity rate than Der p1. Knowing molecular sensitization profiles contributes to better diagnosing and selection of allergen immunotherapy.

Keywords

Allergens, asthma, rhinitis, immunoglobulin E, prevalence

Introduction

The prevalence of asthma and allergic rhinitis is increasing worldwide.[1,2] In Portugal the prevalence of asthma ranges from 10% to 16% and allergic rhinitis from 29% to 33%.[3–5]

Both conditions frequently have an allergic aetiology. These diseases show a positivity of specific IgE sensitization against inhalant allergens, like house dust mites, pollens and even fungus.[6,7] The components of house dust mites are the main cause of sensitization in this population.[8,9] In the Mediterranean area, one of the most significant fungus in respiratory allergy is *Alternaria alternata*. Other allergens like grass pollens, *Parietaria* and *Olea europea*, also have an important role in respiratory allergy.[10]

When allergic rhinitis and asthma co-exist, the patients are usually sensitized to more allergen molecules than patients with only asthma.[8,11–15] Studies also indicate that allergic rhinitis is a risk factor for asthma[16,17] and asthma prevalence is related with the severity and duration of rhinitis.[18]

The IgE sensitization patterns towards aeroallergens and their molecular components have an important role in the study of patients with respiratory allergy. They are useful in the diagnosis and selection of the most adequate immunotherapy.[7,19–21] However, the prevalence of the different aeroallergens and the differences of the molecular IgE sensitization profiles of the patients with asthma and/or rhinitis was not intensively studied in the Portuguese population.

The aim of this study is to evaluate the prevalence of specific IgE sensitization to common aeroallergens and their allergen molecules, like *Dermatophagoides pteronyssinus* and *farinae*, grass pollens, *Olea europaea* pollen and *Alternaria alternata*, in an adult population and identify the patterns associated to asthma and/or rhinitis.

Patients and Methods

We conducted a cross-sectional study, using an existing database of patients from the Clinical and Laboratory Analysis of the Coimbra Hospital and University Centre (CHUC) located in the central region of Portugal.

We selected a sample of patients with allergic rhinitis and/or asthma from the Coimbra University Hospital's Immunoallergology Department who underwent serum tests for aeroallergens' specific IgE (sIgE) between January 1st of 2018 and January 1st of 2020. Then we selected patients who had at least one positive test in the different specific IgEs. We considered a positive test when serum level of sIgE was >0.35 IU/ml and a negative test when the value was ≤0.35 IU/ml. Measurements that were above the upper limit of the detected range were considered as having a value of 100 IU/ml. Patients that received allergen specific immunotherapy were excluded.

At the end, 993 patients were selected for this study, from which 57.4% were females and 42.6% were males, with a mean age of 30.0 ± 13.6 years, ranging from 12 to 83 years. We divided the patients into two groups, according to the clinical information. One group included the patients with only allergic rhinitis, and the other group the patients with asthma, from which some of them also had rhinitis.

The aeroallergens' sIgEs that were analysed included: two house dust mites (HDM) - *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae;* grass pollens*, Olea Europaea, Parietaria judaica* and *Alternaria alternata.*

From the previous sample, we selected a subgroup of patients who also had information about specific IgE values to some allergens' molecules such as: Der p1, Der p2, Der p10, Phl p1, Phl p4, Phl p5, Phl p7, Phl p12, Ole e1, Ole e7, Ole e9 and Par j2. This subgroup includes 303 patients, from which we studied the molecular pattern of sensitization.

This study was approved by the Ethics Committee of the Faculty of Medicine from the University of Coimbra.

The statistical analysis was performed with IBM SPSS Statistics (Version 26). IgE values are presented as geometric means with standard deviations (SD) and categorical values are presented as frequencies and percentages. The threshold for statistical significance was established at a value of $p<0.05$.

Results

The studied population comprised two groups, 635 patients had only allergic rhinitis (63.9%) and 358 patients had asthma (36.1%), from which 247 (67.3%) of them had also rhinitis. The mean age was 29.5 ± 13.4 years in the group with rhinitis and 30.86 ± 13.9 years in the group with asthma.

The frequency of aeroallergens' sensitization, the mean value of sIgE with standard deviation, the maximum and the minimum values are shown in Table I. Most of the patients were sensitized to mites. Patients sensitized to mites or grasses had the highest means of sIgE values.

The sensitization pattern of the population analysed had the following distribution: 78% had positive sIgE to mites, 44% to grass pollens, 14% to olive, 9% to *Parietaria* and 3% to *Alternaria*.

Table I Frequency of allergen-sensitized patients to mites, grass pollens, *Olea europeae*, *Parietaria* and *Alternaria alternata* and their mean, maximum and minimum values of sIgE (IU/ml).

	N	Minimum	Maximum	Mean	Std. Deviation
Mites	776	0.36	100	31.9739	33.3654
Grass pollens	437	0.36	100	24.9957	30.94842
Olea europaea	140	0.36	100	6.7065	16.38606
Parietaria	99	0.36	100	14.8643	22.09541
Alternaria alternata	32	0.4	54.7	13.1216	11.91555

The values of sIgE between gender were not statistical different (p>0.05) in any of the aeroallergens. In Table II, when comparing sIgE values between the group of patients with allergic rhinitis and the group with asthma, we found statistically significant differences in patients sensitized to mites (p=0.001), grasses pollens (p=0.044) or *Alternaria* (p=0.003), in contrast with patients sensitized to *Parietaria* or olive. Asthmatic patients had higher mean values of sIgE to house dust mites and *Alternaria* (37.1 ± 35.3 IU/ml and 25.5 ± 16.7 IU/ml respectively) and patients with rhinitis had a higher mean of sIgE to grass pollens, with a value of 27.0 ± 32.5 IU/ml.

Table II Descriptive statistics, means, medians and standard deviations of sensitized patients to house dust mites, grass pollens, *Olea Europaea*, *Parietaria* and *Alternaria alternata* sIgE (IU/ml) in rhinitis and asthma groups. Comparison between groups, with p value.

Disease		Mites sIgE	Grass sIgE	*Olea* sIgE	*Parietaria* sIgE	*Alternaria* sIgE
Rhinitis	Mean	28.1415	27.0382	7.3730	15.9440	10.2742
	N	473	297	96	70	26
	Std. Deviation	31.6819	32.5265	18.1615	23.5622	8.6898
	Median	15.7000	10.7000	1.8200	5.9250	8.4050
Asthma	Mean	37.1451	20.6628	5.2523	12.2583	25.4600
	N	303	140	44	29	6
	Std. Deviation	35.2713	26.8993	11.6652	18.1842	16.6695
	Median	25.9000	8.1100	1.3400	6.3900	23.0500
Total	Mean	31.9739	24.9957	6.7065	14.8643	13.1216
	N	776	437	140	99	32
	Std. Deviation	33.3654	30.9484	16.3861	22.0954	11.9156
	Median	19.0500	10.6000	1.6900	5.9800	9.6650
Rhinitis vs. Asthma	F	12.112	4.066	0.504	0.568	10.291
	p value	0.001	0.044	0.479	0.453	0.003

Then, we selected a subgroup of 303 patients who had results of sIgE to molecular components of some aeroallergens. The highest positivity rates were seen in Phl p1 (72.2%), Der p2 (66.7%) and Der p1 (54.7%), whereas other molecular components had lower positivity rates (Table III).

From the patients allergic to mites, 64 patients had positivity to Der p1 (54.7% in a total of 117 patients), 74 patients to Der p2 (66.7% in a sample of 111 patients) and 5 patients to Der p10 (14.7% in 34 patients).

Among the group of patients allergic to grass pollens, Phl p1 is the most common allergen (72.2%), followed by Phl p5b with 38.9%, Phl p7 with 13% and Phl p12 with 21.1% (108 patients had test to Phl p1, 95 patients to Phl p5b, 23 patients to Phl p7 and 71 patients to Phl p12). From the group of patients allergic to olive, 12 patients (20.7%) had positivity to Ole e1, 3 patients (14.3%) to Ole e7 and none to Ole e9 (58 patients had values of sIgE to Ole e1, 21 to Ole e7 and 21 to Ole e9). From a total of 29 patients, 8 had positivity to Par j2 (27.8%).

Table III Frequency and percentage (%) of patients sensitized to Der p1, Der p2, Der p10, Phl p1, Phl p5b, Phl p7, Phl p12, Ole e1, Ole e7, Ole e9 and Par j2.

	Der p1	Der p2	Der p10	Phl p1	Phl p5b	Phl p7	Phl p12	Ole e1	Ole e7	Ole e9	Par j2
Frequency	64	74	5	78	37	3	15	12	3	0	8
Percent	54.7	66.7	14.7	72.2	38.9	13.0	21.1	20.7	14.3	0.0	27.6
Total	117	111	34	108	95	23	71	58	21	21	29

We also studied if there were differences in the positivity to these molecular allergens when comparing patients with asthma versus patients with rhinitis (Table IV). When analysing Der p1, Der p2 and Der p10 we can identify that the percentage of positive tests was similar in both groups. In the molecular components of grasses, we observe that they were mostly positive in patients with rhinitis. The percentage of positivity for Ole e1 is higher in patients with rhinitis, and Ole e7 and Par j2 higher in patients with asthma.

Table IV Frequency and percentage (%) of patients sensitized to Der p1, Der p2, Der p10, Phl p1, Phl p5b, Phl p7, Phl p12, Ole e1, Ole e7 and Par j2 in patients with asthma and patients with rhinitis.

Disease		Der p1	Der p2	Der p10	Phl p1	Phl p5b	Phl p7	Phl p12	Ole e1	Ole e7	Par j2
Rhinitis	N	35	44	3	57	26	3	13	9	1	1
	Percent	54.7	59.5	60.0	73.1	70.3	100.0	86.7	75.0	33.3	33.3
Asthma	N	29	30	2	21	11	0	2	3	2	2
	Percent	45.3	40.5	40.0	26.9	29.7	0.0	13.3	25.0	66.7	66.7
Total	N	64	74	5	78	37	3	15	12	3	3

From the patients with sensitization simultaneously to grasses and olive (55 patients), 21 patients had exclusively sensitization to species allergens Phl p1 and/or Phl p5 and/or Ole e1 (corresponding to 38.2%). The other patients (61.8%) had associated positivity to one cross-reactivity allergen like Phl p7 and/or Phl p12 and/or Ole e7 and/or Ole e9 or had negativity to all species allergens.

Discussion

We found a proportion of patients with asthma and rhinitis that is consistent with other studies, in which most of the patients with allergic asthma had also rhinitis.[1]

House dust mites, grass pollens and olive were the most prevalent aeroallergens in our population, as is demonstrated in the GA2LEN skin test study I,[22] which could be justified by the climate of the region and flora.[22,23] House dust mites had the highest mean value of sIgE of all allergens.

The most important aeroallergens in asthmatic patients were house dust mites and in patients with rhinitis grass pollens, reenforcing the fact that outdoor allergens were more closely related to allergic rhinitis and indoor allergens were commonly associated to the development of asthma. This finding is consistent with the literature.[1,7,15] The values of sIgE to HDM is also higher in patients with asthma.

Asthmatic patients also had higher means of sIgE to the fungus *Alternaria*, and as seen in other studies,[8] this sensitization in asthma patients is associated with poor asthma control.[24]

When analysing the molecular allergens, the highest sensitization rates were to Phl p1 (72.2%), Der p2 (66.7%) and Der p1 (54.7%). When comparing both disease groups, the rate of sensitization to molecular components of *Dermatophagoides pteronyssinus* is similar in both groups, showing that this allergen is important in both diseases. Concerning grass pollens' components, the highest positivity rate is observed in patients with rhinitis which is in accordance with the results of sIgE for this allergen.[6] In olive molecular allergens, sensitization to Ole e1 is higher in patients with rhinitis.

Our study suggests that Der p2 is the most important molecular allergen of HDM in our population. This is an interesting finding, since most of previous studies identify Der p1 as the most prevalent HDM molecular. This finding had similarities to what was found in Spain for a cut off value of 0.35 KUA/L, where they found a slightly higher sensitization rate to Der p2 (82.6% to Der p1 and 83.3% for Der p2).[9] But different from what was seen in other studies, like in China, where within the *Dermatophagoides pteronyssinus* Der p1 had the highest positivity rate.[14,25]

Another mite component, Der p10, had a positivity of sIgE of 14.7%, which is concordant with the literature.[25,26] Although we had few patients with positivity to this allergen, it may be interesting to carry out studies with more patients, to evaluate if there is a relation to asthma or rhinitis, since there were studies that show that Der p10 could be a relevant risk factor for mite-induced asthma.[26]

As seen in previous studies, most of the patients sensitized to grass pollens had sIgE to Phl p1, followed by the positivity to Phl p5b and Phl p12 (profilin).[23,27]

In our study, the presence of a reasonable rate of patients sensitized simultaneously to grass pollens and olive who had only positivity to at least one species allergen, namely to Phl p1, or Phl p5 or Ole e1 is an interesting finding, since it is reported that distinguishing sensitization to grass pollens and olive is difficult, due to the presence of cross-reactive allergens in pollens. Therefore, the use of the molecular sensitization pattern could be a useful tool in this differentiation.[28]

This study reveals some limitations, as the studied population could not be representative of the Portuguese allergic population, but only of the population in the central region of Portugal. The diagnosis of asthma or rhinitis was made by the clinicians that required the laboratory test. Since we could not confirm the diagnosis, it may have led to possible misclassifications. We consider rhinitis as allergic rhinitis, but some of the labelled cases could correspond to non-allergic rhinitis. Also, we did not have much epidemiologic information about the patients, only gender and age, and as a result we did not know how similar were the phenotypes of both defined groups (asthma vs rhinitis). And in some cases, we could not be sure if the serum samples were collected before any treatments.

In conclusion, our study provides new insights into the patterns of allergic sensitization of the Portuguese population. It identifies the most prevalent aeroallergens in this population, Phl p1, Der p2 and Der p1, that could be helpful in the study of sensitized patients. This study also identifies a different sensitization pattern for asthma and rhinitis, namely higher rates of sensitization to HDM in asthmatic patients and grass pollens in patients with rhinitis. As allergic diseases could suffer changes over time, it could be interesting to do a longitudinal study of the patients, studying the possible evolution of the pattern of sensitization over time.

Conflict of interests

The authors declare that they have no conflict of interests.

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Anexo

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GUIDE FOR AUTHORS

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