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Allergic sensitization to Storage Dust Mites: a prospective study of patients with respiratory allergy

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Key words

Storage Dust Mite; Dust Mite Allergy; indoor allergens; atopy; mite sensitization.

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Summary

Objective. *To describe the prevalence of allergic sensitization to Storage Dust Mites (SDM); access whether the place of living and occupational exposure were determinants for SDM sensitization and study association between Lepidoglyphus destructor and other SDM sensitization.* ***Methods.*** *Prospective analysis of patients evaluated for suspected allergic rhinitis and/or asthma that performed Skin Prick Tests (SPT) to SDM between January and December 2018 in our Department.* ***Results.*** *Two hundred consecutive patients were evaluated for rhinitis and/or asthma in our outpatient consultation; 123 (61.5%) presented positivity for at least one SDM; 68.3% were female and the mean age was 33.1 ± 12.12. Lepidoglyphus destructor (69.9%) was the most prevalent, followed by Tyrophagus putrescentiae (50.4%), Blomia tropicalis and Glycyphagus domesticus (48.8%) and Acarus siro (24.4%). Living in a rural place was not associated with a higher prevalence of sensitization to SDM, except for Acarus siro ($p = 0.032$), and working in a place with storage areas was not associated with sensitization to any of SDM. Sensitization to Lepidoglyphus destructor was associated with sensitization to Blomia tropicalis, Glycyphagus domesticus and Tyrophagus putrescentiae ($p < 0.005$), but not with Acarus siro.* ***Conclusions.*** *Our study suggests that our population, independently of their occupational exposure and place of residency, are sensitized to SDM and that evaluation of sensitization to SDM should be considered as standard practice.*

Impact statement

Sensitization to storage dust mites seems to be more relevant than previously thought and its evaluation should be considered as standard practice.

Introduction

Storage Dust Mites (SDM) are *Acari* that belong to the suborder *Astigmata,* and the dominant families are *Glycyphagidae*, *Echimyopodidae* and *Acaridae.* Common species of storage mites include *Tyrophagus putrescentiae* (*Tyr p*) and *Acarus siro* (*Aca s*) in the family *Acaridae*, *Lepidoglyphus destructor* (*Lep d*) and *Glycyphagus domesticus* (*Gly d*) in the family *Glycyphagidae*, and *Blomia Tropicalis* (*Blo t*) in the family *Echimyopodidae* (1, 2).

Allergy and sensitization to House Dust Mites (HDM), such as *Dermatophagoides pteronyssinus* (*Der p*) and *Dermatophagoides farinae* (*Der f*), are well known and described in several studies as relevant allergens in allergic patients (2-4). SDM sensitization

has mainly been related to rural occupational exposure, considering they are common in grain and foodstuff storage (5, 6). Searching for specific allergens such as *Blo t* is recommended in tropical countries (7), however, recommendations regarding testing for other SDM are still lacking. Although the importance of sensitization to SDM in the setting of allergic disease is not completely understood, some studies report that storage mites may induce symptoms of asthma and rhinoconjunctivitis in sensitized individuals in both rural and urban settings (8).

In 2011 a Portuguese group analyzed 1349 samples of dust from Portuguese houses of all the country's territory in order to study the prevalence of HDM and intensity of allergic exposure in Portuguese houses (9). Data from this study highly contributed to nowadays practice concerning skin testing for inhalant allergies as patients are screened for pertinent allergens based on history and geographic location.

Concerning Porto region, *Der p* was the most predominant specie (95.3%), while *Der f* was present in a small percentage of samples (13.1%). Regarding SDM, *Led p* was also frequently isolated (46.1%) on the samples from this region. The higher prevalence of *Lep d* and also other SDM was hypothesized to be related with changes in home environment concerning temperature and humidity (9).

However, patient's allergen exposure is not limited to home and outdoor environment and the occupational exposure should also be taken into account. A study conducted along the Iberian region, that included 3225 patients (aged 10-50 years old) with allergic rhinitis concluded that, in the North of Portugal, sensitization rates to dust mites were according to the follow: *Der p* 85%; *Der f* 80%, *Lep d* 72%, *Aca s* 55%, *Gly d* 58%, *Tyr p* 61% and *Blo t* 51% (10). Considering different regions of Portugal, *Der p* (89.5%) and *Der f* (41.2%) were the most prevalent in the Lisbon region, *Der p* (78.2%) and *Lep d* (76.4%) in Portalegre (south interior), *Der p* (92.3%) and *Lep d* (65.4%) in Évora (south interior). Overall, in the south regions, the most prevalent mite was *Der p* followed by *Lep d*. *Lep d* was also common in samples collected in Coimbra (40%) and Leiria cities (40.8%) (west central regions) (9). *Blo t* revealed one of the lowest occurrence frequencies in Portugal's mainland (average frequency of 3.1%) but expressive rates in the Azores (77.5%) and Madeira (51.8%) (Portuguese islands) (9). *Blo t* has been described as the most important and ubiquitous mite species in tropical and subtropical regions of the world whose clinical importance has also been increasingly recognized over the years (11, 12).

The objective of the present study was to describe the pattern of sensitization to SDM in a group of patients with respiratory allergies, and study the association between the sensitization profile and place of living (rural or urban), workplace (with storage area or without storage area) and also the association between *Lep d* and other SDMs sensitizations.

Materials and methods

Population and study design

We performed a prospective analysis including 200 consecutive adult patients (≥ 18 years) living in Porto district, observed for suspected allergic rhinitis and/or asthma between January and December 2018 in our Allergy and Clinical Immunology Outpatient Clinic at Centro Hospitalar Universitário do Porto.

There were included adult patients, sensitized at least to one SDM, with symptoms of rhinitis and or asthma. The exclusion criteria were: absence of SDM sensitization and history of previous immunotherapy.

Allergic diseases were assessed through standardized questionnaires, and the diagnosis of allergic rhinitis and asthma were in accordance to current guidelines, Allergic Rhinitis and its Impact on Asthma (ARIA) (13) and Global Initiative for Asthma (GINA) (14).

We collected patients' data regarding to age, gender, occupation and work-related exposure (with storage area or without storage area), residence (urban or rural), allergic disease diagnosis (rhinitis and/or asthma, atopic dermatitis, conjunctivitis). Patient's occupation was considered as "with storage area" in the follow professions/activities: farmworking, bakering and working in places with warehouses. Allergic sensitization was determined by SPT to 15 allergens included in the standard screening panel used in our clinic (Leti©): *Der p, Der f, Lep d*, Cat, Dog, *Blatella germanica*, mixture of cultivated grass pollen, *Olea europea, Betula verrucosa, Alternaria alternata, Parietaria judaica, Plantago lanceolata, Cladosporium spp., Aspergillus fumigatus*; 0.9% saline and 10 mg/mL histamine solution were used for negative and positive controls, respectively. We added the following SDM: *Acarus siro, Blomia tropicalis, Tyrophagus putrescentiae* and *Glycyphagus domesticus*. SPTs were carried out by trained nurses following a standardized protocol, with readings after 15 minutes. Positivity was considered if the mean wheal size was 3 mm greater than the negative control (15).

The study was conducted according to ethical standards established in the Declaration of Helsinki and was approved by the Ethics Committee of Centro Hospitalar Universitário do Porto. Informed consent was obtained from all participants before enrolment in the study.

Descriptive and statistical analysis

For descriptive analysis, categorical variables were presented as numbers and percentages and continuous variables using mean, standard deviation and minimum and maximum values. Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA, version 22.0).

Student's t-test, Chi-square test and Fisher Exact test were used to investigate the level of association among variables at the significance level of $p < 0.05$.

Results

From a total of 200 patients evaluated for rhinitis and/or asthma in our outpatient consultation, 123 (61.5%) presented sensitization to at least one SDM (**table I**).

In the group of patients that presented sensitization to at least one SDM, there was a predominance of the female gender (84, 68.3%) and mean age of the patients was 33.10 ± 12.12 (minimum 18, maximum 72). Regarding to place of residence, the majority of patients lived in urban areas (85, 69.1%) and work in places without storage areas (110, 89.4%).

Those without SDM sensitization, 77 (38.5%), 52 (67.5%) were female and the mean age was 44.84 ± 14.01 (minimum 18, maximum 70). Considering the place of residence, the majority of patients lived in urban areas (45, 58.4%) and worked in places without storage areas (61, 79.2%). Rhinitis was diagnosed in 64 patients (83.1%) and asthma in 30 (39%). Sensitization to *Der p* was present in 10 (13%) and to *Der f* in 9 (11.7%).

Concerning family and personal history of those with SDM sensitization, the majority of patients presented a positive family history of allergic disease (87, 70.7%) and rhinitis was the most common diagnosis among observed patients (119, 96.7%), followed by asthma (57, 46.3%), conjunctivitis (31, 25.2%) and atopic dermatitis (12, 9.8%). The presence of rhinitis and asthma was observed in 53 patients (43.1%). Regarding to sensitization patterns, *Der p* was the most prevalent mite found (97, 78.9%) followed by *Der f* (93, 75.6%), *Lep d* (86, 69.9%), *Tyr p* (62, 50.4%), *Blo t* and *Gly d* (both in 60 patients, 48.8%) and *Aca s* (30, 24.4%). In comparison with patients with SDM sensitization, patients without SDM sensitization are older (p = 0.007), show a higher frequency of occupational exposure, with no statistical significance (p = 0.326), less frequency of asthma (p = 0.091), with no statistical significance and also lower sensitization rates to *Der p* (p = 0.000) and *Der f* (p = 0.000).

Considering the different age groups, we didn't find an association between sensitization to *Lep d*, *Tyr p*, *Blo t*, *Gly d* and for *Aca s* with any of the groups (p < 0.05).

Sensitization to *Aca s* was superior in patients from urban areas (p = 0.032). For the remaining SDM, the prevalence of sensitization was also higher in the rural areas but with no statistically significant differences (**table II**).

Considering sensitization profiles according to the workplace (**table III**), no statistically significant differences were found in sensitization rates to any of SDM when comparing to those who work in places without storage areas.

Finally, we studied if sensitization to *Lep d* was associated with positivity for other SDM (**table IV**) and that showed positive results for *Blo t*, *Gly d* and *Tyr p*, were an association with statistical significance was found (p = 0.001), but the same was not applicable for *Aca s* (p = 0.166).

Table I *- Demographic and clinical data of the patients with positive SPT to at least one SDM (n = 123) and without SDM sensitization (n = 77).*

Variables	With SDM sensitization	Without SDM sensitization
N	123 (61.5%)	77 (38.5%)
Age (mean; SD; min and max)	33.10 (SD 12.12; min 18, max 72)	44.84 (SD 14.01; min 18; max 70)
Age (intervals)	[18-30] – 73]30-65] – 119]65 - 72] – 8	
Gender (M/F)	39 (31.7%)/84 (68.3%)	25 (32.5%)/52 (67.5%)
Geography (Residence)		
Urban	85 (69.1%)	45 (58.4%)
Rural	38 (30.9%)	32 (41.6%)
Occupational exposure		
Storage	13 (10.6%)	16 (20.8%)
Non-storage	110 (89.4%)	61 (79.2%)
Family history of allergic diseases	87 (70.7%)	34 (44.2%)
Disease characteristics		
Rhinitis	119 (96.7%)	64 (83.1%)
Asthma	57 (46.3%)	30 (39%)
Rhinitis and Asthma	53 (43.1%)	20 (25.9%)
Conjunctivitis	31 (25.2%)	15 (19.5%)
Atopic dermatitis	12 (9.8%)	2 (2.5%)
Sensitization (SPT)		
Der p	97 (78.9%)	10 (13%)
Der f	93 (75.6%)	9 (11.7%)
Lep d	86 (69.9%)	0 (0%)
Tyr p	62 (50.4%)	0 (0%)
Blo t	60 (48.8%)	0 (0%)
Gly d	60 (48.8%)	0 (0%)
Aca s	30 (24.4%)	0 (0%)

Discussion

The panel of allergens used for testing patients with suspected respiratory allergic diseases depends on the allergen exposure of the area of residence and, according to Global Allergy and Asth-

Table II *- Sensitization profiles according to place of residency (rural vs urban).*

	Rural	Urban	P-value
Sensitization			
Der p	29 (76.3%)	68 (80%)	0.644
Der f	29 (76.3%)	64 (75%)	0.903
Lep d	30 (78.9%)	56 (65.9%)	0.144
Tyr p	23 (60.5%)	39 (45.9%)	0.133
Gly d	21 (55.2%)	39 (45.9%)	0.336
Blo t	19 (50%)	41 (48.2%)	0.856
Aca s	14 (36.8%)	16 (18.8%)	**0.032**

ma European Network, in relation to mites, it should include *Der p* and *Der f* (16-18). SPT is described as being highly specific and sensitive, 70-95% and 80-97%, respectively, to diagnose inhalant allergies (19).

Table III *- Sensitization profiles according to workplace (with storage areas vs non-storage areas).*

	Storage	Non-storage	P-value
Sensitization			
Der p	11 (84.6%)	86 (78.2%)	0.734
Der f	10 (76.9%)	83 (75.5%)	1.000
Lep d	11 (84.6%)	75 (68.2%)	0.340
Aca s	3 (23.1%)	27 (24.5%)	0.606
Blo t	6 (46.2%)	54 (49.1%)	0.538
Gly d	5 (38.5%)	55 (50%)	0.431
Tyr p	7 (53.8%)	55 (50%)	0.793

Portuguese population is potentially exposed to a wide number of other mite species besides *Der p* and *Der f* (9, 10, 20), and the standard panel for SPT used in our consultation, which includes *Der p, Der f and Lep d,* may fail to recognize possible relevant sensitizations, such as *Tyr p*, *Gly d* and *Blo t*, especially in those who present sensitization to *Lep d*. In our study, 61.5% of the patients screened were sensitized to at least one SDM, being *Lep d* (69.9%) the most common, followed by *Tyr p* (50.4%), *Blo t* and *Gly d* (both 48.8%), results which are similar to those found in other series in the north of Portugal (10, 20).

Table IV *- Association between Lep d sensitization and sensitization to other SDM.*

	Lep d **negative**	***Lep d*** **positive**	P-value
Sensitization			
Blo t	9 (15%)	51 (85%)	**0.001**
Gly d	9 (15%)	51 (85%)	**0.001**
Tyr p	9 (14.5%)	53 (85.5%)	**0.001**
Aca s	6 (20%)	24 (80%)	0.166

Although sensitization to SDM is commonly associated with living in rural areas and working in places with storage areas (5, 6, 21), in our study we didn't find an association between living in rural areas and a higher sensitization rate for SDM, except for *Aca s.* Considering the workplace, we also did not find an association with working in places with storage areas and higher sensitization rates for SDM, comparing to those working in places without storage areas for all SDM. These findings led us to question whether the concept of "storage dust mites" will be soon subject of review. As the geographic and seasonal distributions of dust mites are determined by their need for adequate humidity, while their distribution within substrates is further determined by their avoidance of light (22); these results could be related to climate changings that occurred over the past years, which in turn can have determined different conditions for SDM proliferation. Another possibility is the cross-reactivity between different mite species. These two assumptions could explain why the differences in workplace and residency place were not statistically significant.
Due to their taxonomic proximity, mites of the same family share several proteins with great homology. Thus, in the mites belonging to the *Pyroglyphidae* family, there is a very high cross-reactivity between *Der p* and *Der f,* and, although in a smaller proportion, there is also a relevant cross-reactivity between *Dermatophagoides* and *Euroglyphus*. In the mites belonging to the *Glycyphagidae* family, there is a high cross-reactivity between *Lepidoglyphus* and *Glycyphagus* and moderate reactivity between these two mites and *Blomia* and *Tyrophagus,* the latter already belonging to the *Acaridae* family. In this family *Acaridae* there is also a moderate reactivity between the genera *Acarus* and *Tyrophagus* (2, 23).
Finally, we addressed whether being sensitized to *Lep d* showed or not association to sensitization to other SDM and we conclude that sensitization to *Lep d* is associated with sensitization to *Blo t*, *Gly d* and *Tyr p* ($p < 0.005$), but not with *Aca s*. These findings can also be related with the need for similar conditions for these mites to proliferate or due to molecular cross-reactivity.

Limitations

The study design may limit the results with the inclusion of a small number of patients in only one center. Also, the evaluation of cross-reactivity between different mite species was not performed in order to address whether those sensitization profiles are due to primary sensitizations or cross-reactivity.

More evidence is needed from larger samples in order to help in future decisions concerning screening for SDM.

Conclusions

Our study suggests that our population, independently of their occupational exposure and place of residency, are sensitized to SDM. To date, and except for *Lep d*, there is no robust evidence to support the clinical implications of SDM sensitization in patients living in Oporto district.

In the light of our findings, the screening of storage mites should be considered more routinely, especially in those with *Lep d* sensitization.

A better comprehension of sensitization profiles to SDM, the complement with serum IgEs assays and specific challenge tests, their relation with environmental exposures and their association with allergic disease; are major determinants for understanding the importance of these mites in the course of the allergic disease.

A continuous assessment of the prevalence of SDM in portuguese houses and studies addressing sensitization profiles are needed in order to identify possible relevant allergic sources.

These results alert us for the importance of creation wider SPT standard panels in our clinic, probably including more SDM and that SDM sensitization is probably underestimated in mite allergic patients.

Conflict of interests

The authors declare that they have no conflict of interests.

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