Pollen-induced allergic asthma and rhinoconjunctivitis outcomes clearly differ from seasonal exposure to out of the season in real-life conditions: The LANDSCAPE STUDY

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Asthma and rhinitis are variable diseases with different pheno-endotypes that determine clinical manifestations [1,2]. Sensitization to a specific allergen may involve clinical profiles with significant differences in symptoms, quality of life, and even choice of therapy by specialists [3,4]. However, asthma and rhinitis classifications are based mainly on severity and/or control, forgetting the importance of current or absence of exposure to allergens in the development of symptoms. Also, pure pollen-allergic patients are not appropriately represented in clinical practice guidelines for asthma and rhinitis.

This multicentre, epidemiological, prospective, observational study aims to compare clinical and pathophysiological features during and outside the pollen allergen exposure period in diagnoses allergic asthma and rhinitis adults, with exclusively seasonal symptoms caused by grasses and/or olive tree pollens at the time of inclusion in the study.

We defined patients allergic to grass and/or olive pollens to those sensitized to these pollens by skin-prick test and/or specific-IgE (ImmunoCAP, ThermoFisher-Scientific, Sweden), who presented symptoms exclusively in the pollination season for those pollens in each geographical area. We excluded pregnant women, patients sensitized to occupational and other perennial or seasonal allergens with a simultaneous exposure period to that of grasses and/or olive-tree, those who had received prior immunotherapy or had any other associated nasal or bronchial disease or any morbidity influencing the pollen season records. Patients who had any other sensitizations (in addition to grass

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and/or olive-tree pollens) could be included if they were not clinically relevant, that is, patients did not show symptoms directly related to those other allergens.

Symptoms, lung function (FEV1, FVC, FEV1/FVC), ACT, miniAQLQ, FEno, Visual Analogic Scale (VAS) for rhinitis and conjunctivitis and ESPRINT questionnaire were determined in all patients. Sociodemographic data and clinical variables were assessed for each patient during and out of the pollen season (autumn and winter), named respectively as visit 1(V1) and visit 2(V2).

Patients were included in V1 at least two weeks after being subjected to pollen levels that induce clinical response (>50 grains /mm3 for grasses, >200 grains/mm3 for olive)[5]. Each investigator included consecutively patients with a confirmed diagnosis of seasonal allergic asthma and rhinitis caused by grass/olive-tree pollens, with or without allergic conjunctivitis, according to the diagnostic criteria for asthma[6] and rhinitis[7].

Participation in the study by investigators and patients was voluntary, and patients had to sign an informed consent document. The Ethics Committee of Hospital Universitario La Paz approved the study (SEA-ASM-2014-01).

101 patients were recruited (mean age, 35.79[±10.97] years). Patients were taken treatment, or it was prescribed at V1 in 81.3% of patients with rhinitis and 79.6% of patients with asthma. At the V2, only 2.4% received treatment in the case of rhinitis and 11.3% in the case of asthma. Nevertheless, a significant difference was observed between the visits with respect to markers of severity for rhinitis and asthma: At V1, the percentage of intermittent asthma was 25.5%, mild persistent asthma 28.6 %, moderate persistent asthma 41.8, and severe asthma: 4.1%. At V2, 67% of patients had no asthmatic symptoms, 22.4% presented characteristics compatible with intermittent asthma, 4.1% with mild persistent asthma, 6.1% with moderate persistent asthma, and no patient was classified as severe asthma. At V1, the percentage of mild rhinitis was 22.4 %, persistent 62.2% and severe 14.3 %. At V2, 58,2 % of patients had no rhinitis symptoms, 32,6 % had symptoms consistent with mild rhinitis, 8.2% with moderate rhinitis, and only an 1% with severe rhinitis.

Significant differences were observed between the visits with respect to severity classification for both diseases and for ACT, FEno, MiniAQLQ, FEV1(%), FEV1/FVC

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ratio, VAS for rhinitis and conjunctivitis and ESPRINT questionnaire, but not for FVC values (Table 1).

The results of our study confirm exposure to the allergen as the determining factor for the symptoms of allergic asthma and rhinoconjunctivitis. Furthermore, exposure to allergens can condition the diagnostic profitability of asthma by modifying the results of FEno and lung function.

However, our findings also show that clinical features do not disappear completely in all patients outside the exposure period, as almost one-third of asthmatic patients and 41.8% of those with rhinitis continue to present symptoms, although the severity is clearly lower than V1 Therefore, it seems clear that the allergic response determines clinical manifestations in the respiratory tract, even during periods when the patient is not directly exposed to the allergen responsible for his/her symptoms. Contact with the allergen may cause pathophysiological abnormalities that lead to clinical manifestations [8]. This possibility could prove to be important in circumstances that trigger respiratory symptoms, such as infections or contact with irritants [9].

Furthermore, consistent with the results of similar studies [10], measurement of FEno, as an indicator of the presence of type-2 inflammation [11], also revealed a significant increase during the exposure period, thus indicating that FEno could be a sensitive parameter for determining exposure to the allergen. The FEno value decreased significantly outside the pollen season. In addition, the values of some lung function parameters, such as FEV1, were associated with exposure to the allergen, whereas values such as FVC did not vary significantly, indicating that the presence of clinical manifestations could be more sensitive to limited allergen exposure over time than lung function abnormalities, especially in patients who receive antiasthma treatment.

A potential limitation of the present study is its small sample size. However, the population was very homogenous and patient selection was very strict: patients in whom other possible sensitizations could have had a clinical effect were excluded. The presence of patients sensitized to multiple allergens is common in Spain [12, 13]. Nevertheless, most patients were sensitized only to pollens whose pollination period was markedly seasonal, such as grasses and olive.

In conclusion, most of patients diagnosed with allergic rhinoconjunctivitis and asthma due to sensitization to grass/olive pollens, exclusively experience clinical

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manifestations, lung function abnormalities, and airway-inflammation during the pollen season. However, some few of them continue to experience abnormalities outside the exposure period.

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Conflict of interest

All the authors declare no conflict of interest for this manuscript.

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REFERENCES

1. Moore WC, Meyers DA, Wenzel SE, Teague WG, Li H, Li X, et al. Identification of asthma phenotypes using a clustering analysis in the Severe Asthma Research Program. Am J Respir Crit Care Med. 2010;181:315-23
2. Papadopoulos NG, Bernstein JA, Demoly P, Dykewicz M, Fokkens W, Hellings PW, et al. Phenotypes and endotypes of rhinitis and their impact on management: a PRACTALL report. Allergy. 2015;70: 474-94.
3. Valero A, Quirce S, Dávila I, Delgado J, Domínguez-Ortega J. Allergic respiratory disease: Different allergens, different symptoms. Allergy. 2017;72: 1306-16.
4. Domínguez Ortega J, Quirce S, Delgado J, Dávila I, Martí-Guadaño E, Valero A. Diagnostic and therapeutic approaches in respiratory allergy are different depending on the profile of aeroallergen sensitization. Allergol Immunopathol (Madr). 2014;42:11-8.
5. Pola Pola J, Subiza Garrido-Lestache JM, GArcia Menaya JM, Porcel Carreño SL. Pólenes de interés en Alergología en nuestro medio. En: Tratado de Alergología. Tomo I. Madrid Ergon¸2015. P 247-274.
6. GEMA 2009 (Spanish guideline on the management of asthma). Executive Committee GEMA 2009. J Investig Allergol Clin Immunol. 2010;20 Suppl 1:1-59.
7. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008;63 Suppl 8:8–160.
8. Schatz M, Rosenwasser L. The allergic asthma phenotype. J Allergy Clin Immunol Pract. 2014;2:645-8
9. Ramsahai JM, Hansbro PM, Wark P. Mechanisms and management of asthma exacerbations. Am J Respir Crit Care Med. 2019;199:423-32
10. Bake B, Viklund E, Olin AC. Effects of pollen season on central and peripheral nitric oxide production in subjects with pollen asthma. Respir Med 2014;108:1277-83.

Accepted

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doi: 10.18176/jiaci.0544

11. Silkoff PE, Laviolette M, Singh D, FitzGerald JM, Kelsen S, Backer V, et al. Identification of airway mucosal type-2 inflammation by using clinical biomarkers in asthmatic patients. J Allergy Clin Immunol 2017;140:710-9.

12. Migueres M, Dávila I, Frati F, Azpeitia A, Jeanpetit Y, Lhéritier-Barrand M, et al. Types of sensitization to aeroallergens: definitions, prevalences and impact on the diagnosis and treatment of allergic respiratory disease. Clin Transl Allergy. 2014;4:16.

13. Ojeda P, Sastre J, Olaguibel JM, Chivato T; investigators participating in the National Survey of the Spanish Society of Allergology and Clinical Immunology Alergológica 2015. Alergológica 2015: A National Survey on Allergic Diseases in the Adult Spanish Population. J Investig Allergol Clin Immunol. 2018;28:151-64

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