Seasonal Administration of Omalizumab in Patients With Uncontrolled Asthma and Sensitization to Olive Pollen

Serrano P[1,2,3], Navas A[1,2,3], Ruiz-León B[1,2,3], Herrero L[4], Rondón C[3,5], Jurado A[1,2,3], Moreno-Aguilar C[1,2,3]

[1]*Department of Immunology and Allergy, Reina Sofia University Hospital, Córdoba, Spain*

[2]*Maimonides Biomedical Research Institute of Córdoba (IMIBIC)/ Reina Sofia University Hospital/University of Córdoba, Córdoba, Spain*

[3]*National Network ARADyAL, Carlos III Health Institute, Madrid, Spain*

[4]*Department of Information, Computer Systems and Archives Systems (Contabilidad Analítica), Hospital Infanta Margarita, Cabra, Córdoba, Spain*

[5]*Biomedical Research Institute of Málaga (IBIMA)/Allergy Unit Hospital Regional Universitario de Málaga, Málaga, Spain*

J Investig Allergol Clin Immunol 2021; Vol. 31(5): 436-438
doi: 10.18176/jiaci.0657

Key words: Asthma. Omalizumab. Olive pollen. Seasonal.

Palabras clave: Asma. Omalizumab. Polen de olivo. Estacional.

Sensitization to olive pollen leads to the development of asthma. In areas with high pollen counts, such as the southern Mediterranean, sensitization to Ole e 7 leads to more severe asthma [1-3].

In Cordoba, olive and grasses are major sources of pollen, causing rhinoconjunctivitis and asthma during the spring season. Only olive pollen reaches extreme counts (>20 000 grains/m^3/y).

Allergen immunotherapy (AIT) is indicated when sensitization is clinically relevant and pharmacologic control of asthma is not satisfactory. When sensitization to Ole e 7 is single or predominant, AIT is associated with a higher incidence of adverse reactions [4]. Moreover, poor control of minor allergens in most extracts constitutes an additional difficulty [5]. Therefore, AIT could be inappropriate for patients predominantly sensitized to Ole e 7.

Omalizumab has been widely used to treat severe perennial allergic asthma [6]. However, few data are available on severe asthma due to pollen sensitization. The aim of this study was to analyze the results of a pilot seasonal treatment with omalizumab under conditions of daily clinical practice in patients with uncontrolled seasonal asthma, strong sensitization to minor olive allergens, and exposure to high pollen counts.

Retrospective data from 33 patients (84.4% women; mean [SD] age, 31.4 [12.35] years) were selected based on the following: (*1*) high exposure to olive pollen; (*2*) moderate-severe persistent asthma [7]; (*3*) poor control of symptoms in 2 previous springs according to the GEMA guidelines [7]; (*4*) relevant sensitization to minor olive allergens (mean [SD]

sIgE: Ole e 1, 24.5 [26.5]; Ole e 7, 67.5 [70.8]; and Ole e 9, 19.5 [28.6]). Further data are supplied in Supplementary Figure 1); (*5*) off-label treatment with omalizumab for 16 weeks (March-June 2013, which included the olive pollination season) in daily clinical practice (according to the manufacturer's product information) [8].

The only exclusion criterion was sensitization to other pollens.

Interestingly, 66% of patients included had received olive immunotherapy, with a poor clinical response and unacceptable rate of adverse reactions.

Clinical variables were collected from medical records, as follows: (*1*) daytime symptoms (dyspnea, cough, wheezing, chest tightness), activity limitation, night symptoms/awakening, need for relief medication (short-acting ß$_2$-agonists [SABA]), exacerbations, maintenance medication (inhaled corticosteroids with or without long-acting ß$_2$-agonists, antileukotrienes, other); (*2*) qualitative severity parameters (need for oral corticosteroids, emergency visits).

A summarized asthma control index (SACI) was established based on the GEMA guidelines [7], with the following values:

- SACI 2 (well-controlled asthma): absence of night symptoms, activity limitations, exacerbations, daytime symptoms ≤2 d/wk, need for SABA ≤2 times/wk, FEV_1 ≥80% of theoretical value.
- SACI 1 (partially controlled asthma): at least 4 out of 6 conditions from SACI 2.
- SACI 0 (badly controlled asthma): fewer than 4 out of 6 conditions from SACI 2.
- The SACI was obtained monthly from March to June 2013 at the visits for administration of omalizumab. The statistical analysis was based on the worst SACI obtained for each patient. The overall spring SACI for 2011 was obtained from medical records.

We performed a descriptive analysis of variables and compared the 2013 and 2011 seasons (before and after omalizumab). The 2012 season was not considered in order to avoid possible bias due to lower pollen counts (Supplementary Figure 2). The McNemar test was used to measure the consistency of changes in the SACI and severity parameters (need for oral corticosteroids, emergency visits). A bivariate analysis (χ^2) was performed based on the dependent variable (SACI) and the independent variables sex and age. Significance was set at α=0.05.

The study protocol was approved by the local ethics committee, and informed consent was obtained from all patients or their legal representatives.

Omalizumab doses ranged from 150 mg/4 wk to 600 mg/2 wk. The most frequent dose was 450 mg/2 wk (27.2% of patients). Both the SACI and severity parameters were significantly improved (*P*<.001) after treatment with omalizumab (Table). Detailed data are shown in Supplementary Figure 3. The best results were obtained from patients in GEMA step 6 (Supplementary Table 1). The χ^2 test revealed no significant differences between SACI and the independent variables (sex, *P*=1.000; age, *P*=.688).

This study showed that seasonal treatment with omalizumab improves disease control in patients with uncontrolled asthma due to olive pollen allergy. Patients in the study had poorly controlled asthma during the olive pollen season but remained mostly asymptomatic for the rest of the year. Nevertheless, guidelines do not classify seasonal asthma as perennial based on severity.

Asthma control is a complex health problem from the perspective of its indicators. In the present study, omalizumab had an impact on all patients by reducing the need for oral corticosteroids and the number of visits to the emergency department. Patients experienced fewer symptoms with fewer drugs and medical interventions. It remains unknown whether, in addition to better controlling asthma, omalizumab has a possible preventive role in future worsening, as well as potential cost savings [9].

Previous studies on seasonal treatment with omalizumab in pollen-allergic patients with rhinitis [10,11] have revealed an improvement in symptoms and quality of life and reduced use of rescue medication [10,11].

An important aspect of this study was that patients were treated with omalizumab for only 16 weeks. If we had overlooked the seasonal nature of asthma and treated patients based on degree of severity and control, we would have used 6708 prefilled syringes (150 mg) (€2 931 328.92). In contrast, we only consumed 516 syringes (€225 486.84).

In summary, reduced drug administration and better control of severe pollen-induced asthma through seasonal treatment with omalizumab results in an appropriate cost-benefit balance compared with a perennial schedule. Health care systems should not ignore this protocol.

The main limitations of the study were its retrospective design and the small sample size. Nevertheless, our results

Table. Summarized Asthma Control Index Based on the GEMA Grading and Severity Variables Before and After Receiving Omalizumab

	SACI	No. (%)	McNemar	OCS No. (%)	McNemar	Emergency, No. (%)	McNemar
Before omalizumab (2011)	2	0		10		12	
	1	11 (33.3%)		(30.3%)		(36.3%)	
	0	22 (66.7%)					
After omalizumab (2013)	2	12 (36.4%)	21 (*P*<.001)	5	16.2	2	17.2
				(15.1%)	(*P*<.001)	(6%)	(*P*<.001)
	1	14 (42.4%)	2.777 (*P*=.095)				
	0	7 (21.2%)	0.88 (*P*=.345)				

Abbreviation: OCS, oral corticosteroids; SACI, summarized asthma control index.

highlight the importance of classifying asthma and may enable improved allocation of therapeutic resources.

The omalizumab schedule we describe in patients with severe asthma and a complex olive pollen sensitization profile may lead to better control of asthma and, therefore, could represent a successful alternative therapy for affected patients. However, more studies are needed to validate this proof of concept.

Acknowledgments

The authors thank Carmen Galan for providing data on the pollen concentration in each year of the study.

Funding

This paper was supported by an unrestricted grant from Menarini.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

1. Barber D, De La Torre F, Feo F, Florido F, Guardia P, Moreno C, et al. Understanding patient sensitization profiles in complex pollen areas: A molecular epidemiological study. Allergy Eur J Allergy Clin Immunol. 2008;63(11):1550-8.
2. Alcántara M, Sáenz de San Pedro B, Cañada C, Muñoz MA, Jimeno L, Villalba M, et al. Steps towards clarifying the clinical relevance of minor olive allergen in areas. J Investig Allergol Clin Immunol. 2017;27(2):138-40.
3. Porcel Carreño S, Gómez Nieves E, Fernández-Caldas E, Abel Fernández E, Cases B, Tudela JI, et al. Immunochemical and physical quantitation of grass and olive pollen allergens and correlation with asthma admitions in Cáceres, Spain. J Investig Allergol Clin Immunol. 2020;30(5):334-9.
4. Peñuelas E, Serrano P, Barasona MJ, Saiz V, Fernandez L, Moreno C. Sensitization to minor allergens has a direct influence on the outcome of subcutaneous immunotherapy in olive-allergic patients. J Investig Allergol Clin Immunol. 2016;26(3):202-4.
5. Duffort O, Palomares O, Lombardero M, Villalba M, Barber D, Rodríguez R, et al. Variability of Ole e 9 allergen in olive pollen extracts: Relevance of minor allergens in immunotherapy treatments. Int Arch Allergy Immunol. 2006;140(2):131-8.
6. Normansell R, Walker S, Milan SJ, Walters EH NP. Omalizumab for asthma in adults and children. Cochrane Database Syst Rev. 2014;1(1):2014;1(1):CD003559.
7. SEPAR. GEMA. Guia Española para el Manejo del Asma [Internet]. 2009. Available from: www.gemasma.com
8. http://www.ema.europa.eu/ [Internet]. Available from: http://www.ema.europa.eu/docs/es_ES/document_library/EPAR_-_Product_Information/human/000606/WC500057298.pdf
9. Entrenas Costa LM, Casas-Maldonado F, Soto Campos JG, Padilla-Galo A, Levy A, Álvarez Gutiérrez FJ, et al. Economic Impact and Clinical Outcomes of Omalizumab Add-On Therapy for Patients with Severe Persistent Asthma: A Real-World Study. Pharmacoecon Open. 2019;3(3):333-42.
10. Nagakura T, Ogino S, Okubo K, Sato N, Takahashi M Ishikawa T. Omalizumab is more effective than suplatast tosilate in the treatment of Japanese cedar pollen-induced seasonal allergic rhinitis. Clin Exp Allergy. 2008;38(2):329-37.
11. Okubo K, Ogino S, Nagakura T, Ishikawa T. Omalizumab is Effective and Safe in the Treatment of Japanese Cedar Pollen-induced Seasonal Allergic Rhinitis. Allergol Int. 2006;55(4):379-86.

Manuscript received June 2, 2020; accepted for publication November 23, 2020.

Berta Ruiz León
Department of Immunology and Allergy
Reina Sofia University Hospital
Avenida Menéndez Pidal, s/n
Córdoba, Spain
E-mail: rulebe@gmail.com