ORIGINAL ARTICLE

Quality of Life in Patients With Respiratory Allergy Is Influenced by the Causative Allergen

J Delgado,[1*] I Dávila,[2*] J Domínguez-Ortega,[3] S Quirce,[4] E Martí-Guadaño,[5] A Valero[6]

[1]Allergy UGC, Hospital Virgen Macarena, Sevilla, Spain
[2]Immunoallergy Department, IBSAL-Hospital Universitario de Salamanca, Salamanca, Spain
[3]Allergy Unit, Hospital Universitario de Getafe, Getafe, Spain
[4]Allergy Department, Hospital La Paz Institute for Health Research (IdiPAZ), and CIBER de Enfermedades Respiratorias, CIBERES, Madrid, Spain
[5]Allergy Department, Hospital Moisès Broggi, Sant Joan Despí, Barcelona, Spain
[6]Pneumology and Allergy Department, Clinical and Experimental Respiratory Immunoallergy, IDIBAPS, CIBERES, Hospital Clínic, Barcelona, Spain

[*]Both authors contributed equally to this work

Abstract

Objective: We aimed to analyze health-related quality of life (HRQOL) in adults with newly diagnosed respiratory allergy according to the sensitization profile for relevant aeroallergens in their usual area of residence.
Methods: We performed a cross-sectional, epidemiological, observational, descriptive, multicenter study in allergy clinics in Spain. The sample comprised adults diagnosed with rhinitis, asthma, or both caused by significant allergens in their residential area (olive and/or grass pollen or house dust mite). Allergic rhinitis was classified according to the Allergic Rhinitis and its Impact on Asthma guidelines; asthma was classified according to the Guía Española para el Manejo del Asma (Spanish Guideline on the Management of Asthma). HRQOL was studied according to the ESPRINT-15 questionnaire and Mini Asthma Quality of Life Questionnaire. Control of asthma was measured using the Asthma Control Questionnaire 5.
Results: We studied 1437 patients. Rhinitis was the most common respiratory disease. The HRQOL of rhinitis patients was lower in those sensitized to olive pollen only and in those with combined sensitization to olive and grass pollens. HRQOL associated with rhinitis was worse in patients diagnosed with both rhinitis and asthma than in patients diagnosed with rhinitis only. Asthma patients sensitized to olive pollen or olive and grass pollens had worse HRQOL.
Conclusions: In our study population, the HRQOL of patients with respiratory allergies varied with the allergen responsible for symptoms. In patients with rhinitis, the presence of asthma significantly worsened rhinitis-associated HRQOL.

Key words: Cross-sectional. Epidemiological. Descriptive. Respiratory allergies. Health-related quality of life.

Resumen

Objetivo: Valorar si la afectación en la calidad de vida relacionada con la salud (CVRS) de los pacientes adultos diagnosticados por primera vez de enfermedad respiratoria alérgica se ve influida por el alérgeno causante.
Método: Se realizó un estudio epidemiológico, multicéntrico, transversal, observacional y descriptivo en consultas de Alergología de España. Se incluyeron pacientes adultos diagnosticados de rinitis y/o asma alérgica causados por los alérgenos significativos de su lugar de residencia (polen de olivo y/o gramíneas o ácaros del polvo doméstico). La rinitis alérgica se clasificó según los criterios de la guía ARIA y el asma según la guía GEMA. La CVRS se estudió según los cuestionarios ESPRINT-15 y miniAQLQ. El control del asma se midió utilizando el cuestionario ACQ5.
Resultados: Se evaluaron un total de 1.437 pacientes. La rinitis fue la enfermedad respiratoria alérgica más común. La CVRS fue menor en pacientes monosensibilizados al polen de olivo y en los que presentaban polisensibilización a polen de olivo y gramíneas. La CVRS asociada a la rinitis fue menor en pacientes con diagnóstico de rinitis y asma, comparados con los pacientes diagnosticados solo de rinitis.
Conclusiones: Los pacientes asmáticos sensibilizados al polen de olivo o a polen de gramíneas y olivo presentaban peor calidad de vida. Los pacientes alérgicos a los pólenes presentan peor calidad de vida que los pacientes alérgicos a los ácaros. La presencia de asma en pacientes con rinitis empeora la CVRS asociada a la rinitis.

Palabras clave: Transversal. Estudio epidemiológico. Descriptivo. Alergia respiratoria. Alérgenos. Calidad de vida.

Introduction

Health-related quality of life (HRQOL) is defined as the patient's perception of the effects of a specific disease or the use of a certain treatment on different aspects of his/her life, particularly the consequences for the patient's physical, emotional, and social well-being [1]. When measuring HRQOL, data are collected directly from the patient and, as such, differ somewhat from those obtained with the conventional measurements used in standard practice (clinical and instrumental tests). Consequently, they must be quantified independently. In recent years, the role of HRQOL as a tool for evaluating numerous diseases has expanded, particularly for chronic conditions.

Allergic respiratory diseases, such as rhinitis and asthma, are chronic diseases with a high prevalence in the general population. The prevalence of allergic rhinitis ranges between 10% and 30%, while that of asthma ranges between 4% and 10% [2]. Both diseases are closely related: 20% to 50% of patients with allergic rhinitis have asthma, whereas 30% to 90% of asthma patients have rhinitis [3]. In addition, allergic respiratory diseases have a severe impact on HRQOL [4,5].

The importance of measuring HRQOL in these diseases is underscored by recent guidelines on the management of rhinitis and asthma, which consider it an essential parameter in the classification of the severity of the disease [6,7]. Various instruments have been developed or adapted for measuring quality of life in the Spanish population. These include the ESPRINT-15 rhinitis questionnaire and the Mini Asthma Quality of Life Questionnaire (Mini-AQLQ). Both have been validated in several studies [8-11] and have proven effective in the study of HRQOL in patients with rhinitis and asthma.

In allergic respiratory diseases, the variations inherent to the specific characteristics of the sensitizing allergens and the patient's geographical area of residence can lead to variations in symptoms, which can in turn affect HRQOL. However, these factors (place of residence and sensitization to the relevant allergen) have not been studied in depth. In Spain, as in other countries, the 2 main groups of predominant allergens are pollen and house dust mite [12]. While pollen-sensitized patients have symptoms during the pollen season (usually around 2 or 3 months of the year) and generally remain asymptomatic for the rest of the time, patients sensitized to dust mite are symptomatic all year round, although some seasonal variations may be observed.

In this study, we analyze HRQOL and asthma control in patients attending an allergy clinic for the first time in Spain and determine whether there are significant differences between allergy to pollen and allergy to house dust mite.

Methods

Design

We performed a cross-sectional, epidemiological, observational, descriptive, multicenter study in Spain. The patients were adults with respiratory allergy (rhinitis or asthma) attending an allergy clinic for the first time.

Population and Sample

This study was carried out between March 2010 and June 2010. Each allergy specialist included 11 consecutive patients newly diagnosed with rhinoconjunctivitis, asthma, or both at the allergy clinic. Patients were included if they fulfilled the following criteria: *(1)* age >18 years and signed informed consent to participate; *(2)* sensitization to grass and/or olive pollen or to house dust mite; *(3)* inclusion during the symptomatic period; and *(4)* at least 2 years' residence in the province where they were included. The study was approved by the Clinical Research Ethics Committee of Hospital Clínic, Barcelona, Spain.

Patients with lung diseases other than asthma or nasal diseases other than rhinitis were excluded, as were pregnant women. Patients sensitized to animal dander, storage mites, molds, occupational allergens, and types of pollen other than those specified with exposure-related symptoms were also excluded. Administration of specific immunotherapy against any of the study allergens at any time was also an exclusion criterion.

Variables

We collected sociodemographic variables (age, sex, and place of residence). Rhinitis was diagnosed according to the Allergic Rhinitis and its Impact on Asthma guidelines [7] and classified according to the modifications of Valero et al [8]. Asthma was diagnosed and classified according to the Guía Española para el Manejo del Asma (GEMA: Spanish Guideline on the Management of Asthma) [6]. Sensitization to the most significant allergens (olive or grass pollen or house dust mite) in each geographical area was determined by skin prick testing, which was sometimes performed in combination with serum specific immunoglobulin (Ig) E determination. Any positive skin test result (wheal ≥3 mm greater than the negative control) or any specific IgE value >0.35 kU_A/L for any aeroallergen was considered a positive result. Patients with serum specific IgE and/or positive skin test results and a compatible clinical picture were considered allergic. Histamine dihydrochloride (10 mg/mL) was used as a positive control and 0.9% saline solution as a negative control.

Quality of Life Questionnaires

ESPRINT-15 is a rhinitis-specific HRQOL questionnaire that has been validated in Spain [10]. It consists of 15 questions covering symptoms (5 items), daily activities (3 items), sleep (3 items), psychological effects (3 items), and well-being (1 item). The questions were answered on a 6-point Likert scale. The lowest HRQOL corresponds to a score of 6 [4,6].

The Mini-AQLQ has been validated for the Spanish population [9] and contains 15 items in 4 dimensions: limitation of normal activities (4 items), symptoms (5 items), emotional function (3 items), and environmental stimuli (3 items). HRQOL scores range between 1 (maximum limitation) and 7 (no limitation).

Asthma Control Questionnaire

Asthma control was assessed using the Asthma Control

Questionnaire 5 (ACQ5), which consists of 5 questions on symptom control scored on a scale of 0 to 6. The value 0 represents excellent asthma control [10]. This instrument has also been validated in the Spanish population [11]. Recent studies have established the cutoff for uncontrolled asthma at >1 [12]. Asthma was classified as controlled, partially controlled, and uncontrolled according to the criteria of GEMA [6].

Statistical Analysis

The clinical characteristics of patients with allergic respiratory disease were analyzed using summary statistics. Demographic patterns according to allergic disease and sensitization to various allergens were analyzed using contingency tables and the χ^2 test. Quantitative variables were studied using a *t* test for factors with 2 levels or analysis of variance for factors with >2 levels. The Fisher exact test was used for tables with very low values (<5).

Statistical significance was set at $P<.05$.

Results

Sociodemographic Characteristics

A total of 200 allergy specialists from throughout Spain recruited 1437 patients of both sexes with a diagnosis of respiratory allergy due to grass and/or olive pollen or house dust mite. Of the 1437 patients, 150 met at least 1 of the exclusion criteria. Of the evaluable patients (n=1287), 46.5% were men and 53.5% women, with a mean (SD) age of 34.18 (11.8) years (range, 18-80 years). The coast was the usual place of residence for 354 patients (27.76%) and inland for 921 (72.24%). As for the type of residence, 7.18% lived in a rural area, 20.69% in semiurban areas, and 72.13% in urban areas.

Clinical Characteristics

A family history of rhinitis was recorded in 47.04% of patients. Rhinitis affected 58.6%, rhinitis and asthma 38.77%, and asthma without associated rhinitis only 2.63%. The average time from onset of symptoms was 7.13 years (median, 4.9 years) for rhinitis and 5.15 years (median, 2.64 years) for asthma. Further information can be consulted elsewhere [13].

Grass pollen was the relevant allergen in 25.3% of patients, olive pollen in 7.87%, and house dust mite in 20.54%. The remaining patients were significantly sensitized to both grass and olive pollens.

Quality of Life and Asthma Control

ESPRINT-15 questionnaire (Table 1): The ESPRINT-15 questionnaire showed good capacity for discrimination between degrees of severity of rhinitis, with a higher score corresponding to greater severity ($P<.0001$). Patients with rhinitis associated with asthma had lower HRQOL than patients with a diagnosis of rhinitis alone ($P=.0016$). Patients sensitized to pollen had lower HRQOL than patients sensitized to house dust mite ($P=.0123$). This finding was particularly significant in patients sensitized to olive pollen only ($P=.0003$) and in those sensitized to both grass and olive pollen ($P=.0168$)

Table 1. HRQOL in Rhinitis Patients (ESPRINT-15)

	Mean (SD)	*P* Values
Sensitization by Significant Allergen		
Grass	2.54 (1.27)	.2299
Olive	2.68 (1.27)	.0003
Grass and olive	2.65 (1.25)	.0168
House dust mite	2.36 (1.3)	.0123
Sensitization to Grass, Olive, or Grass and Olive		
Grass only	2.45 (1.27)	
Olive only	2.79 (1.26)	.0480
Grass and olive	2.66 (1.27)	
Area of Residence		
Coastal	2.62 (1.2)	.0863
Inland	2.46 (1.3)	
Severity of Rhinitis in Patients With Rhinitis Without Asthma		
Mild	1.23 (0.77)	
Moderate	2.41 (1.06)	<.0001
Severe	3.76 (1.16)	
Rhinitis With or Without Asthma		
Patients with rhinitis	2.41 (1.22)	
Patients with rhinitis and asthma	2.67 (1.33)	.0016
Severity of Rhinitis in Patients With Rhinitis and Asthma		
Mild	1.61 (1.28)	
Moderate	2.63 (1.15)	<.0001
Severe	4.02 (1)	

Abbreviation: HRQOL, health-related quality of life.

No significant differences in HRQOL associated with the type or area of residence were observed.

Mini-AQLQ (Table 2): The Mini-AQLQ questionnaire showed a good correlation with asthma severity, according to the GEMA guidelines, with a significantly lower score being obtained as the severity of the asthma increased ($P<.0001$). A good correlation was also observed with the degree of asthma control ($P=.0001$).

Type of sensitization also influenced HRQOL: patients sensitized to olive pollen had a significantly lower HRQOL than patients sensitized to grass pollen or house dust mite. Living inland was also associated with poorer HRQOL.

The score obtained from the questionnaire also correlated significantly with asthma control according to the GEMA guidelines ($P<.0001$).

ACQ5 questionnaire (Table 3): A statistically significant relationship was observed between the ACQ5 questionnaire score and asthma severity and control according to the GEMA guidelines ($P<.0001$). A statistically significant correlation (–0.75) with the Mini-AQLQ questionnaire was obtained: the higher the ACQ5 score, the lower the Mini-AQLQ score (Figure).

Table 2. HRQOL (Mini-AQLQ) in Asthma Patients

	Mean (SD)	*P* Values
Sensitization by Significant Allergen		
Grass	4.92 (1.23)	.3335
Olive	4.68 (1.26)	.0003
Grass and olive	4.72 (1.24)	.0119
House dust mite	4.95 (1.26)	.0969
Sensitization to Grass, Olive, or Grass and Olive		
Grass only	5.25 (1.23)	
Olive only	4.33 (1.26)	.0001
Grass and olive	4.69 (1.22)	
Area of Residence		
Coastal	5.14 (1.2)	.0210
Inland	4.83 (1.3)	
Severity of Asthma According to GEMA Guidelines		
Intermittent	5.55 (1.13)	
Persistent-mild	4.93 (1.11)	<.0001
Persistent-moderate	4.41 (1.14)	
Persistent-severe	3.47 (0.99)	
Asthma Control According to GEMA Guidelines		
Well controlled	5.51 (1.14)	
Partially controlled	4.62 (1.08)	<.0001

Abbreviation: AQLQ, Asthma Quality of Life Questionnaire; GEMA, Guía Española para el Manejo del Asma (Spanish Guideline on the Management of Asthma); HRQOL, health-related quality of life.

Table 3. Evaluation of Asthma Control (ACQ5): Correlation With Asthma Severity and Control According to the GEMA Guidelines

	Mean (SD)	*P* Values
Severity of Asthma According to GEMA Guidelines		
Intermittent	0.98 (0.96)	
Persistent-mild	1.69 (1.09)	<.0001
Persistent-moderate	2.19 (1.14)	
Persistent-severe	3.72 (0.61)	
Asthma Control According to GEMA Guidelines		
Well controlled	0.97 (0.9)	
Partially controlled	2.01 (1.08)	<.0001
Poorly controlled	2.89 (1.12)	

Abbreviation: AQLQ, Asthma Quality of Life Questionnaire; GEMA, Guía Española para el Manejo del Asma (Spanish Guideline on the Management of Asthma); HRQOL, health-related quality of life.

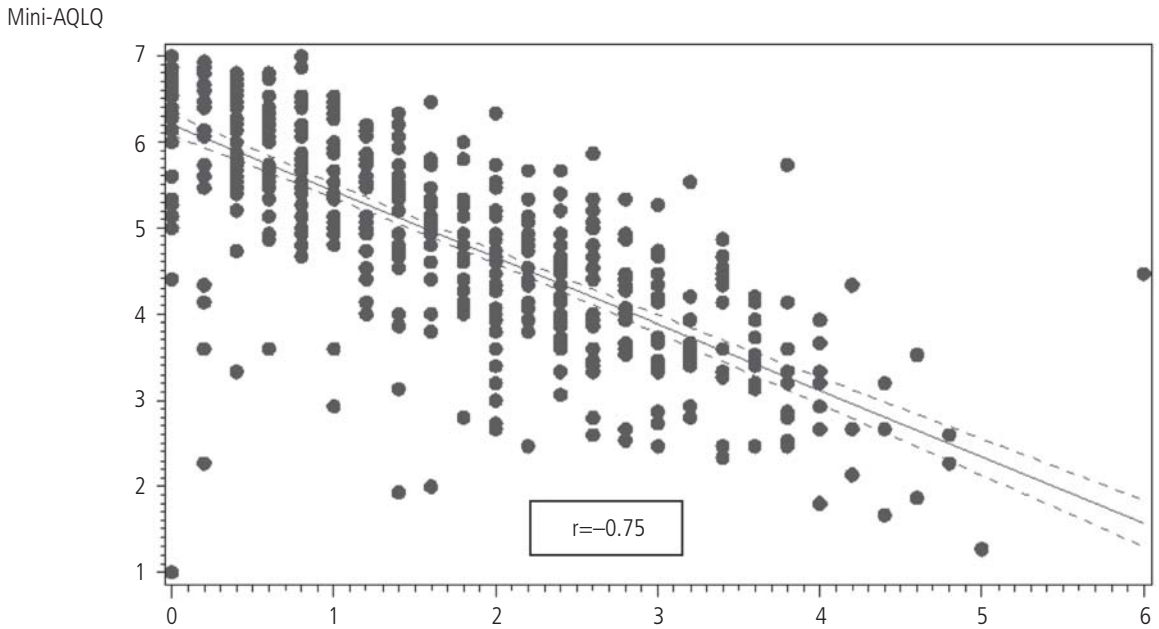

Figure. Correlation between data obtained from the Mini-AQLQ and ACQ5 in asthmatic patients. AQLQ indicates Asthma Quality of Life Questionnaire; ACQ5, Asthma Control Questionnaire 5.

Discussion

The questionnaires used in this study proved to be effective tools for evaluating quality of life in a large sample of patients diagnosed with allergic respiratory disease: the ESPRINT-15 questionnaire score correlated significantly with severity of rhinitis, while the Mini-AQLQ and ACQ5 correlated significantly with severity and control of asthma according to the GEMA guidelines.

For the last few years, HRQOL and asthma control have been included as habitual variables in the evaluation of the clinical symptoms and progress of patients diagnosed with allergic rhinitis and bronchial asthma; however, no specific studies have established an association between these variables and the etiological agent. In this sense, our results indicate that sensitization to the relevant allergens of the geographical area do affect the quality of life of patients with respiratory allergy: patients sensitized to pollen had a significantly worse HRQOL than patients sensitized to house dust mite. It is well known that the geographical variability of respiratory allergens leads to variations in both the incidence and clinical manifestations of diseases caused by these clinical entities [14,15]. In a recent study carried out in Italy, Milani et al [16] showed that patients sensitized to olive, *Parietaria*, or ragweed pollen had more severe clinical symptoms than patients sensitized to tree or cypress pollen. As such, it seems obvious that the type of allergen causing the symptoms can affect the HRQOL of allergic patients.

In our work, the HRQOL of allergic rhinitis patients sensitized to olive pollen only was more affected than that of patients sensitized to grass pollen or house dust mite only. Similar results were observed for asthma: the Mini-AQLQ questionnaire indicated that asthma patients sensitized to olive pollen had poorer HRQOL than those sensitized to grass or house dust mite. Patients (asthma and rhinitis) sensitized to both grass and olive pollen had poorer HRQOL, with values lying between those for patients sensitized to olive pollen only and those sensitized to grass pollen only. This effect may be due to the characteristics of olive pollination in our environment, which is explosive in nature, reaching very high levels in a few days, in contrast with the more gradual pollination of grasses.

Curiously, seasonal allergens such as pollen affect HRQOL to a greater degree, while perennial allergens such as dust mite produce symptoms that are more tolerable for patients, whether patients with rhinitis or with both rhinitis and asthma. These results may be related to different environmental allergen levels: the increase is usually more intense in the case of pollen, whereas house dust mite allergens only remain in the air when turbulence is produced, thus reducing the total amount of allergen inhaled to usually less than 10 ng per day [17]. Furthermore, pollen allergens can remain suspended in the air for long periods of time [18]. Moderate pollen levels inside the home have also been observed during the pollen season (over 10 μg of the major *Lolium* allergen per gram of house dust), enough to induce symptoms in an allergic patient, even in those who avoid going outdoors on the days of highest pollen counts [19]. Nevertheless, it should be remembered that pollen-allergic patients were evaluated during the pollination period. In addition, patients sensitized to house dust mite are symptomatic throughout the year, thus reducing their perception of symptoms to a greater extent than pollen-allergic patients, whose exposure is sudden and limited [20]. In this respect, Bousquet et al [21] showed that disease severity had more effect than duration. This finding agrees with the data recorded in our study.

Consistent with other studies showing significant variations in sensitization to aeroallergens according to geographical area [22], we observed that patients who lived in inland regions have poorer HRQOL, probably because of different sensitization patterns [22]. The Iberian study, which was carried out in over 3000 patients in Spain and Portugal, showed that, in Spain, sensitization to house dust mite was more common in coastal regions than in the center, while sensitization to pollen was more common in inland areas [23]. This could explain the differences observed in our study between inland regions and coastal regions.

Finally, our results confirm that the presence of asthma worsens the HRQOL of patients diagnosed with rhinitis, regardless of the allergen involved. This finding was also recorded in studies recently performed in Spain [24,25] and could be explained by inflammatory mechanisms common to both respiratory diseases [26].

One possible limitation of our study is that both severity and degree of control can affect HRQOL, thus hindering interpretation of results. Nevertheless, overall, neither the severity nor the degree of asthma control was significantly different between patients sensitized to pollen and patients sensitized to house dust mite (data not shown) [13].

The results of this study suggest that the HRQOL of patients with allergic respiratory diseases is affected by the sensitizing allergens. Thus, etiological diagnosis is useful for recommending avoidance measures and should be considered a major determinant of HRQOL in these patients.

Funding

This study was supported in part by Laboratorios ESTEVE.

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

1. The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. Soc Sci Med. 1995;41:1403-9.
2. Von Mutius, E. The rising trends in asthma and allergic disease. Clin Exp Allergy. 1998;28 Suppl 5:45-9.
3. Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. J Allergy Clin Immunol. 2000;106:S201-5.
4. Juniper EF. Quality of life in adults and children with asthma and rhinitis. Allergy. 1997;52:971-7.
5. Gerth van WR. Quality of life, should we bother? Allergy. 2003;58:284-6.
6. Executive Committee GEMA 2009. GEMA 2009 (Spanish

guideline on the management of asthma). J Investig Allergol Clin Immunol. 2010;20 Suppl 1:1-59.
7. Bousquet, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, Zuberbier T, Baena-Cagnani CE, Canonica GW. 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 86:8-160.
8. Valero A, Alonso J, Antepara I, Baró E, Colas C, del Cuvillo A, Ferrer M, Herdman M, Martí-Guadaño E, Monclús L, Mullol J, Navarro-Pulido AM, Navas C, Sastre J, Baltasar M, Bartra J, Serrano C, Cardona V, Castillo JA, Cerda MT, Cistero A, Conejero A, Davila I, Escudero C, Hernandez E, Vereda A, Fernandez B, Mencia J, Fernández J, Florido J, Quiralte J, Guardia P, Malek T, Montoro J, Orta JC, Oehling A, Pascual MJ, de la Parte B, Raga E, Rubira N, Ranea S, Rivas P, Serra J, Tabar A. Development and validation of a new Spanish instrument to measure health-related quality of life in patients with allergic rhinitis: the ESPRINT questionnaire. Value Health. 2007;10:466-77.
9. Sanjuàs C, Alonso J, Sanchís J, Casan P, Broquetas JM, Ferrie PJ, Juniper EF, Antó JM. [The quality-of-life questionnaire with asthma patients: the Spanish version of the Asthma Quality of Life Questionnaire]. Arch Bronconeumol. 1995;31:219-26. Spanish
10. Chabra SK, Kaushik S. Validation of the asthma quality of life questionnaire (AQLQ-UK English version) in Indian asthmatic subjects. Indian J Chest Dis Allied Sci. 2005;47:167-73.
11. Badiola C, Badía X, Sastre J, Olaguibel JM, Lopez-Viña A, Vega JM, Picado C. Evaluación de las versiones simplificadas del Cuestionario de Control del Asma. Med Clin. 2008;131:326-32.
12. Olaguibel JM, Quirce S, Julia B, Fernandez C, Fortuna AM, Molina J, Plaza V. Measurement of asthma control according to global initiative for asthma guidelines: a comparison with the asthma control questionnaire. Respir Res. 2012;13(1):50-60.
13. 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). 2012 Dec 19. pii: S0301-0546(12)00282-0.
14. Moral L, Roig M, Garde J, Alos A, Toral T, Fuentes MJ. Allergen sensitization in children with asthma and rhinitis: marked variations related to age and microgeographical factors. Allergol Immunopathol (Madr). 2008;36:128-33.
15. Togias A. Rhinitis and asthma: evidence for respiratory system integration. J Allergy Clin Immunol. 2003;111:1171-83.
16. Milani M, Pecora S; Rainbow Study Investigator Group. Clinical relevance of non-grass pollens respiratory allergies in Italy and effects of specific sublingual immunotherapy: The Rainbow Trial, a multicentre 3-year prospective observational study. Eur Ann Allergy Clin Immunol. 2011 Aug;43(4):111-6.
17. Platts-Mills T, Erwin EA, Woodfolk JA, Heymann PW. Environmental factors influencing allergy and asthma. Chem Immunol Allergy. 2006;91:3-15.
18. Platts-Mills TAE, Vervloet D, Thomas WR, Aalberse RC, Chapman MD. Indoor allergens and asthma: report of the Third International Workshop. 1997;100:S1-24.
19. Pollart SM, Reid MJ, Fling JA, Chapman MD, Platts-Mills TA. Epidemiology of emergency room asthma in northern California: association with IgE antibody to ryegrass pollen. J Allergy Clin Immunol. 1988;82:224-30.
20. Rodríguez-de la Cruz D, Sánchez-Reyes E, Dávila-González I, Lorente-Toledano F. Airborne pollen calender of Salamanca, Spain, 2000-2007. Allergol Immunopathol (Madr). 2010;38(6):307-12.
21. Bousquet J, Neukirch F, Bousquet PJ, Gehano P, Klossek JM, Bashar Allaf ML. Severity and impairment of allergic rhinitis in patients consulting in primary care. J Allergy Clin Immunol. 2006;17:158-62.
22. Bousquet PJ, Chinn S, Janson C, Kogevinas M, Burney P, Jarvis D. Geographical variation in the prevalence of positive skin tests to environmental aeroallergens in the European Community Respiratory Health Survey I. Allergy. 2008;62:301-9.
23. Pereira C, Valero A, Loureiro C, Davila I, Martinez-Cocera C, Murio C, Rico P, Palomino R. Iberian study of aeroallergens sensitisation in allergic rhinitis. Eur Ann Allergy Clin Immunol. 2006;38:186-94.
24. Navarro A, Valero A, Juliá B, Quirce S. Coexistence of asthma and allergic rhinitis in adult patients attending allergy clinics: ONEAIR study. J Investig Allergol Clin Immunol. 2008;18:233-8.
25. Castillo Vizuete JA, Mullol J. Rhinitis and asthma comorbidity in Spain: the RINAIR study. Arch Bronconeumol. 2008;44:597-603.
26. Gelfand EW. Inflammatory mediators in allergic rhinitis. J Allergy Clin Immunol. 2004;114:S135-8.

Manuscript received September 18, 2012; accepted for publication December 20, 2012.

Julio Delgado Romero

Allergy UGC
Hospital Virgen Macarena
Sevilla, Spain
E-mail: juliodelgadoromero@gmail.com