

Diagnosis and treatment of allergic rhinitis due to house-dust mites in Spain

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ABSTRACT

Background: The prevalence of allergic rhinitis due to house-dust mites (HDMs) is high and increasing. Treatment guidelines and consensus statements are available, but few data exist on how these are followed in clinical practice in Spain. This study was designed to collect data on diagnosis and treatment of allergic rhinitis due to HDMs and adherence to guidelines in Spanish specialized clinical practice.

Methods: In this observational study, patients referred to specialists for a first consultation were collected. Diagnosis of allergic rhinitis due to HDMs was confirmed by skin-prick tests and measurement of specific immunoglobulin E levels. Variables included patient demographics, diagnosis, and treatment. Moreover, investigators answered a questionnaire on their attitudes to allergic rhinitis treatment.

Results: Two hundred forty-seven clinicians collected evaluable data from 519 patients (mean age, 24.8 years; SD, 11.9 years; 54% women) with confirmed allergic rhinitis (86.2% with moderate or severe disease and 70.5% with persistent disease; 40% with concomitant asthma) caused by *Dermatophagoides*. In 85.6% of patients, symptoms had not improved since diagnosis and good disease control was only being achieved in 43.4%. At the study visit, pharmacologic treatment was prescribed in 98.3% and allergen immunotherapy was prescribed in 52.2% of patients.

Conclusion: When patients with HDM-induced allergic rhinitis are referred to an allergy specialist in Spain, they have moderate-to-severe persistent disease and are generally not achieving good control with symptomatic treatment. Allergen immunotherapy is prescribed in approximately one-half of patients. In this representative sample of Spanish allergy specialists, the level of adherence to clinical guidelines in these patients is encouraging.

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According to the Spanish results of the European Community Respiratory Health Survey, the prevalence of allergic rhinitis in Spain was between 12.1 and 17.6%, in 1996.¹ A recent cross-sectional, population-based study, conducted by telephone interviews with randomly chosen adult subjects in countries throughout Western Europe, found a prevalence of clinically confirmable rhinitis of 21.5% in our country.² The study also found that 48% of patients with rhinitis were classified by the investigator as suffering from perennial allergic rhinitis, and the most common allergens were house-dust mites (HDM) and animal dander. The prevalence of this disease is thought to be increasing.³

Several options are available for the treatment of allergic rhinitis. These can broadly be divided into symptomatic relief (pharmacotherapy⁴) and those that aim to modify the underlying disease (allergen immunotherapy⁵). These approaches are often combined with measures to avoid exposure to the allergen.⁶ In addition, patient education is also considered an important component. Consensus statements and clinical guidelines that address the relative merits of these treatments are available.^{3,7}

Despite the high and increasing prevalence of perennial allergic rhinitis, relatively little is known about the approaches used for diagnosis and treatment of the condition or, indeed, the extent of adherence to current clinical guidelines. Navarro *et al.*⁸ investigated the epidemiology of allergic rhinitis (due to any allergen) in patients attending Spanish allergy clinics and collected some data on treat-

ments administered. However, that study did not report disease severity, changes in symptoms over time, or treatment outcomes.

The aim of the present study was to collect data on the diagnosis and treatment of patients with HDM allergic rhinitis who had been referred to Spanish specialists and information on adherence to guidelines in Spanish specialized clinical practice.

METHODS

This cross-sectional study was conducted in normal clinical practice between November 2007 and May 2008. Allergy specialists were selected at random from throughout Spain, with the number of specialists from a given province reflecting the population of that province and the prevalence of sensitization to HDMs (according to internal data). A total of 433 specialists from public and private clinics were randomly selected to participate in the study. Of these, 297 (62.8%) finally agreed to participate, and 247 (52.2%) from 195 different locations, but with a predominance of investigators from humid coastal regions, provided evaluable data on patients with allergic rhinitis caused by HDMs. The majority of the clinicians worked in hospital clinics (71.0%) and 65% of them belonged to the Public Health System. Patients were recruited from all regions of Spain.

Specialists were instructed to recruit consecutive patients meeting the following inclusion criteria: ≥ 5 years of age, first consultation (with the investigator), and diagnosis of allergic rhinitis (with or without bronchial asthma) due to HDMs of the genus *Dermatophagoides*, confirmed by positive skin-prick tests and/or *Dermatophagoides*-specific immunoglobulin E (IgE) of >0.70 kU/L. Patients participating in other epidemiological studies or clinical trials were excluded.

The present study did not interfere in any way with the normal prescribing practice of the participating clinicians. All patients (or the parents/legal guardian in the case of pediatric patients) gave written informed consent for their data to be used in the analysis. Confidentiality of the patients' data was maintained at all times. The study was evaluated and approved by the Ethics Committee of the Hospital Clinic, Barcelona, Spain.

Study Variables

A standard case report form was used to collect data on sociodemographic and clinical characteristics of the patients. Previous and

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Table 1 Demographic and clinical characteristics of the patients with house-dust mite allergic rhinitis included in the study

	<i>n</i> = 519*
Sex	
Male	232 (46.1%)
Female	271 (53.9%)
Type of environment	
Rural	91 (17.6%)
Urban	425 (82.4%)
Family history of respiratory allergies	
Yes	293 (56.6%)
History of other allergic diseases	
Asthma	205 (44.8%)
Atopic dermatitis	53 (11.6%)
Acute recurrent urticaria	19 (4.1%)

*There were missing data for each characteristic.

concomitant diseases including asthma, classified according to the Global Initiative for Asthma definitions,⁹ progress of rhinitis symptoms, and prior therapies administered for rhinitis were retrospectively obtained.

To evaluate the procedures used by the investigators for diagnosing allergic rhinitis, the following data were collected: physical examination (including type of examination when specified, *e.g.*, palpation and auscultation), respiratory function tests, imaging studies, and allergy-specific tests (skin-prick tests and specific IgE). To provide information on treatment patterns for allergic rhinitis, data on the treatments performed (environmental control, pharmacologic agents, and immunotherapy, along with details of each type of therapy) were obtained. In addition, information on any educational measures was also collected.

Physician Attitudes to Patients with Allergic Rhinitis

The investigators were also asked to fill in a questionnaire about their usual approach to management of patients with HDM-induced allergic rhinitis. In addition to physicians' demographic data, the questionnaire requested information on the types of treatments that they habitually prescribed in their clinical practice.

Statistical Analysis

Descriptive statistics were calculated for all of the patient characteristics recorded during the data collection visit. These included means and medians with their corresponding SDs and interquartile ranges for continuous variables and percentages of the total for categorical variables.

RESULTS

Of the 555 patients included by the investigators, 519 (93.5%) had evaluable data. The most common reason for excluding patients from the analysis was lack of allergic sensitization confirmed by positive skin-prick test and/or specific IgE (19 patients; 3.4%).

Demographic characteristics of these patients are summarized in Table 1. The mean age of the patients included in the study was 24.8 (SD, 11.9 years) years (range, 5–75 years) and 31% were <18 years of age. The remaining patients were between 18 and 44 years of age (62.9%). Fifty-four percent were women and a large majority of these patients (82.4%) lived in an urban area.

The characteristics of allergic rhinitis are presented in Table 2. In the assessment of change in symptoms since they first appeared, 85.6% considered that their symptoms were either unchanged, worse, or much worse than at initial diagnosis. According to the Allergic

Table 2 Current characteristics of allergic rhinitis

	<i>n</i> = 519*
Time elapsed since onset of symptoms (yr: mean [SD])	7.6 (7.6)
Percent of patients with duration of ≥ 2 yr	444 (85.5%)
Symptoms	
Sneezing	456 (87.9%)
Runny nose	471 (90.8%)
Itchy nose	427 (82.3%)
Blocked nose	420 (80.9%)
Change in symptoms since onset	
Much better	8 (1.6%)
Better	66 (12.8%)
No change	179 (34.8%)
Worse	223 (43.4%)
Much worse	38 (7.4%)
ARIA classification	
Mild-intermittent	38 (7.5%)
Mild-persistent	32 (6.3%)
Moderate/severe-intermittent	111 (22.0%)
Moderate/severe-persistent	324 (64.2%)

*There were missing data for each characteristic.

ARIA = Allergic Rhinitis and Its Impact on Asthma.

Rhinitis and Its Impact on Asthma (ARIA) classification,³ 86.2% had moderate or severe disease and in 85.5% the duration of allergic rhinitis was ≥ 2 years. Almost one-half of the patients (47.8%) had been referred by the family doctor, and 21.5% attended the specialist on their own initiative (>75% of these in private clinics) and 18.6% were referred by pediatricians.

Diagnostic Workup

The vast majority of patients (494/519; 95.2%) underwent a physical examination, with the most common examination methods being visual inspection (88.5% of the examinations), respiratory auscultation (77.5%), anterior rhinoscopy (80.2%), and palpation (20.2%).

Other diagnostic tests performed included spirometry in 49.9% (history of asthma but not ARIA classification influenced whether this test was performed), blood counts in 41.2%, biochemistry in 25.6%, radiograph of the paranasal sinuses in 17.7%, chest radiograph in 11.9%, peak expiratory flow in 6.0%, rhinomanometry in 5.6%, and acoustic rhinometry in 5.2%. By definition, to be included in the study, patients had to have a positive skin-prick test or positive reaction of specific IgE to *Dermatophagoides*. In the skin-prick test, 166 patients (32%) were sensitized only to *Dermatophagoides*, and 38% were also sensitized to pollen, 25.8% to dog, and 21.8% to cat dander. Thirty-three percent of patients were also sensitized to other mites (*Lepidoglyphus*, *Tyrophagus*, *Acarus*, or *Blomia*). Total and specific IgE were determined in 53.8 and 48.9% of the patients, respectively.

At the study visit, 40.3% of the patients were considered to have asthma by the investigators, based on the additional diagnostic tests. Fifty-seven percent of these patients had intermittent asthma and 33% had mild-to-moderate persistent asthma. Conjunctivitis was diagnosed in 43.7% of the patients.

Treatments

In total, 411/519 patients (79.2%) had received prior therapy for allergic rhinitis before being included in the study. In most cases (80%) this consisted of pharmacologic treatment, which did not achieve a good disease control, according to the patients' perception, in 56.6% of them; furthermore, 34 patients (6.6%) had experienced some sort of adverse drug reaction to previous treatment, the most common being drowsiness (15 patients; 2.9%). The therapeutic alter-

Table 3 Interventions prescribed at the study visit

	<i>n</i> = 519
Allergen avoidance	514 (99.0%)
Lifestyle changes	448 (86.3%)
Physical measures	340 (65.5%)
Chemical measures	56 (10.8%)
Pharmacologic treatment	510 (98.3%)
Oral antihistamine agents	108 (20.8%)
Nasal corticosteroids	36 (6.9%)
Oral antihistamines + nasal corticosteroids	360 (69.4%)
Montelukast	60 (11.6%)
Nasal antihistamine agents	25 (4.8%)
Nasal vasoconstrictors	46 (8.9%)
Chromones	5 (1.0%)
Immunotherapy	273 (52.6%)
Subcutaneous immunotherapy (natural antigen extracts)	131 (25.2%)
Subcutaneous immunotherapy (modified "allergoid" preparations)	47 (9.1%)
Sublingual immunotherapy	95 (18.3%)
Educational measures	478 (92.1%)

natives prescribed at the study visit are summarized in Table 3. Allergen avoidance and pharmacologic treatment were indicated in almost all patients, and educational measures were indicated in >90% and some form of allergen immunotherapy in just over one-half of the sample.

The most widely indicated pharmacologic treatments were oral antihistamine agents and nasal corticosteroids, prescribed in 90.2 and 76.3% of patients, respectively. No use of first-generation antihistamine agents was reported. Other pharmacologic treatments used in more than 5% of the patients were montelukast (11.6%) and nasal vasoconstrictors (8.9%).

Of the patients who were prescribed specific immunotherapy, the most common type was subcutaneous administration, accounting for 65.2% of immunotherapy courses (approximately three-quarters corresponded to natural allergen extracts and the remaining ones corresponded to modified or "allergoid" preparations). Sublingual immunotherapy accounted for 35% of the courses of immunotherapy. When the composition was specified, it comprised a single allergen (*Dermatophagoides pteronyssinus*) in 42.9% of the courses, and this allergen was mixed with *Dermatophagoides farinae* in 43.8% of the courses. On asking the investigators whether they would subsequently prescribe specific immunotherapy for the patients if they did not do so at the initial visit, they answered affirmatively only in case of worsening rhinitis (63.5%) or development of asthma (28.3%).

Attitudes of the Physicians to Treatment

A total of 246 investigators also answered a questionnaire on their approaches and attitudes to treatment of patients with HDM-induced allergic rhinitis in their routine clinical practice.

Pharmacologic treatments were habitually prescribed by all physicians participating in the survey, with the most common types of drugs being oral antihistamine agents and intranasal topical corticosteroids (prescribed by all physicians). When asked how they used pharmacologic treatment, 89 (41%) replied that they only used pharmacologic treatment when the patient was symptomatic and 78 (36%) said they used it at times of most extensive allergen exposure. Forty-nine (23%) prescribed pharmacologic treatment all the year.

Allergen avoidance measures were habitually used by all but one of the investigators included in the study. When asked about the reasons for use of such measures, 45.9% considered that there is sufficient scientific evidence for their use and 79.3% considered that they are effective according to their own personal experience.

DISCUSSION

According to the results of the present study, Spanish allergy specialists are reasonably adherent to the international guidelines^{3,7} in the management of allergic rhinitis caused by HDM, a disease with important individual, social, and economic consequences.¹⁰⁻¹² In the Spanish national health system, patients can only see a specialist if they are referred from primary care. For the most part, if a family doctor is able to control symptoms of rhinitis or those symptoms are mild, then the patient will generally not be referred to a specialist. In this sample in which 65% of the specialists worked in the public sector, patients attended by the Spanish allergy specialists tended to have moderate-to-severe forms of the disease (>80%) with a mean time since onset of 7.6 years and one-half complained of worsening of symptoms since their onset.

The most common diagnostic procedures were skin-prick tests and/or measurement of serum-specific IgE, as recommended by the European Academy of Allergology and Clinical Immunology and ARIA guidelines,^{3,7} although a recent study suggests that skin-prick tests are preferable in patients <30 years of age.¹³ Spanish specialists are aware of the well-known relationship between bronchial asthma and rhinitis,¹⁴⁻¹⁶ and one-half of the patients underwent basal spirometry in line with the ARIA guidelines. The percentage of patients with asthma (40%) was quite similar to that previously reported.^{3,17} The most frequently reported symptoms in our study were runny nose and sneezing. This is in contrast to the findings of the Allergies in America survey, which reported nasal blockage as the most frequent symptom.¹⁸ The discrepancy can perhaps be explained by the fact that 73% of the patients were recruited between January and May when the period of greatest severity of symptoms of allergic rhinitis due to HDM, including nasal congestion, is between October and December.¹⁹

Pharmacologic symptomatic treatment was indicated in almost all patients included in the study and agents were used in combination. Up to 92% of the patients were prescribed oral second-generation antihistamines even though there is still some debate concerning the efficacy of these agents.²⁰ The combination of nasal corticosteroids with oral antihistamines was the most popular treatment among Spanish specialists. This is a surprising finding because nasal corticosteroids are more effective than oral antihistamines²¹ and guidelines recommend their use as first-line treatment for patients with moderate-to-severe symptoms instead of combined therapy with both.^{3,7}

The relatively limited use of montelukast (shown to be effective in seasonal rhinitis²²) in our study could be related to the lack of indication for rhinitis in our country. Nasal vasoconstrictors (decongestants), although acceptable for short-term use, were not widely used because they are generally not recommended for long-term therapy because of the risk of developing rhinitis medicamentosa.²³ Despite the proven efficacy of nasal antihistamine agents,²⁴ these drugs were not widely used, in line with the consensus statement of the European Academy of Allergology and Clinical Immunology,⁷ which recommends their use in mild organ-limited disease.

This survey shows that less than one-half of the patients achieved complete symptom relief with their previous pharmacologic treatment before referral, confirming the need for additional therapeutic measures. Allergen avoidance or environmental control is also recommended in the guidelines,^{3,7} despite the lack of solid scientific evidence in HDM-allergic patients.²⁵ Interestingly, the investigators in the present study, who prescribed allergen avoidance measures in almost all subjects, were largely convinced of the efficacy of these measures in their own experience. This may reflect the difficulty in conducting trials with an acceptable methodology (e.g., difficulties in blinding the intervention) and also the fact that many of the trials testing specific interventions also included general interventions in both arms, thereby diluting any group effect. Leaving aside the question of efficacy, it has been shown that those measures can reduce the level of exposure.²⁶

For patients with clinically relevant IgE-mediated disease, and particularly for those with sensitization to a limited number of aller-

gens, the efficacy of immunotherapy has been shown in numerous clinical trials when administered as a subcutaneous injection,²⁷ although there have been concerns about safety, in particular, anaphylactic reactions.²⁸ Careful patient selection and monitoring by experienced health care professionals is therefore necessary. Sublingual administration is another possibility and its efficacy has been indicated for a number of allergens.²⁹ Some isolated cases of anaphylaxis have been communicated,³⁰ but this route of administration has generally proved safe, even with high-dose regimens.³¹ In our study, only 52% of the patients with allergic rhinitis due to HDM received allergen immunotherapy, even though many of them had moderate or severe disease. A possible explanation for not prescribing immunotherapy may be the difficult etiologic diagnosis in patients sensitized to other perennial allergens (*e.g.*, cats, dogs, and other mites). On the other hand, many specialists might not consider prescribing immunotherapy in the first consultation but would nevertheless prescribe it in subsequent visits, once they confirm the disease severity and response to drug treatment. In the study reported by Navarro *et al.*,⁸ 38% of the patients were prescribed with immunotherapy although that study also included patients sensitized to other allergens besides HDMs.

Educational measures have been shown to help maximize compliance with treatment and optimize outcomes³² and the importance of education has been highlighted in the most recent ARIA update.³ Our results would suggest that Spanish physicians share this concern for education, because 90% practiced some form of educational intervention (*e.g.*, information leaflets and oral explanations about treatment/disease) during the study visit.

In conclusion, allergy specialists in Spain largely follow the recommendations of the main consensus statements and guidelines on diagnosis and treatment when attending their patients. Seemingly as a result of the system for referral to a specialist in the public sector, patients generally have moderate-to-severe and longstanding disease with symptoms that have worsened over time. They often also have asthma, and previous drug symptomatic treatment achieves adequate disease control in less than one-half of the patients. Pharmacotherapies (mainly oral antihistamine agents and nasal corticosteroids) are widely used, but allergen immunotherapy is only used in about one-half of patients; furthermore, some patients with frequent or severe symptoms, worsening symptoms, and inadequate control with pharmacologic treatment do not receive allergen immunotherapy, at least at the first visit.

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