Asthma in Alergológica-2005

S Quirce

Allergology Service, Hospital La Paz, Madrid and Center for Biomedical Research in Respiratory Diseases (CIBER), Spain

Abstract

Background: This study analyses the prevalence and the clinical and therapeutic data on asthma collected in consultations as part of Alergológica-2005.

Material and Methods: A cross-sectional, descriptive, observational, epidemiologic study was carried out.

Results: The prevalence of asthma was 28%, lower than the 35% prevalence observed in the Alergológica-2002 study. The average age of the patients with asthma was 27 years (range 1 to 86). Those affected were children between 5 and 15 years of age and young adults. 55.4% were females. The classification of asthma according to severity was: 57.4% slight, 40.9% moderate and 1.7% serious. 79.8% of patients had extrinsic asthma, 18.7% intrinsic asthma and 1.2% occupational asthma. 43.8% of patients were sensitized to pollens, 41.4% to dust mites and 19.6% to animal epithelia.

In comparison with the first phase of Alergológica, the prescription of immunotherapy fell from 54% to 30%, theophylline from 26% to 0.4%, chromones/ketotifen from 53% to 1.4% and inhaled corticosteroids from 40% to 31.7%. In contrast, combinations of inhaled corticosteroids and long-acting β2-agonists and antileukotrienes, both of which were absent in the first phase of the study, made a great impact in this second phase of the study with figures of 38.5% and 24.4% respectively.

Conclusions: The prevalence of asthma in Alergológica-2005 has diminished in comparison with the first phase of the study. Changes in the therapeutic guidelines are clear such as a reduction in the use of immunotherapy and a notable increase in the prescription of combinations and antileukotrienes.

Key words: Asthma. Allergy. Spirometry. Severe asthma. Corticosteroids. Immunotherapy. Antileukotrienes.

Resumen

Introducción: En este estudio se analiza la prevalencia y datos clínicos y terapéuticos del asma estudiada en consultas de Alergología. Material y métodos: Estudio epidemiológico observacional descriptivo de tipo transversal.

Resultados: La prevalencia de asma fue del 28%, inferior a la prevalencia del 35% observada en *Alergológica* 2002. La edad media de los pacientes con asma era 27 años (rango 1 a 86). Se observa un predominio de niños entre 5 y 15 años y de adultos jóvenes. El 55,4% eran mujeres. La clasificación del asma según la gravedad fue: 57,4% leve, 40,9% moderada y 1,7% grave. El 79,8% de los pacientes tenían asma extrínseca, el 18,7% asma intrínseca, y un 1,2% asma ocupacional. El 43,8% de los pacientes estaba sensibilizado a pólenes, el 41,4% a ácaros y el 19,6% a epitelios de animales.

Respecto a la primera fase de Alergológica, destaca la disminución de la prescripción de inmunoterapia del 54% al 30%, de teofilina del 26% al 0,4%, de cromonas/ketotifeno del 53% al 1,4%, y de los corticosteroides inhalados del 40% al 31,7%. Por el contrario, irrumpen con fuerza en esta fase del estudio las combinaciones de corticosteroides inhalados y agonistas-beta-2 de acción prolongada, con un 38,5%, y los antileucotrienos, con un 24,4%, ambos inexistentes en la primera fase.

Conclusiónes: La prevalencia de asma en las consultas de Alergología ha disminuido respecto a la primera fase. Se observan cambios en las pautas terapéuticas como una disminución de la utilización de la inmunoterapia y una notable prescripción de combinaciones y antileucotrienos.

Palabras clave: Asma, alergia, espirometría, asma grave, corticosteroides, inmunoterapia, antileucotrienos.

Introduction

According to data from the *European Community Health Survey*, carried out in the early 1990s, 4.5% of the population aged between 20 and 44 years had asthma (with extreme values

of 2% and 11.9%) as defined by the presence of characteristic symptoms or the use of anti-asthma medications [1]. In this study, the prevalence rates of asthma in Spain were low although regional variation was considerable: 10% in Albacete, 6.5% in Barcelona, 5% in Galdácano, 14.5% in Huelva and 9.4% in

Oviedo [2]. When bronchial hyperreactivity (as determined by the methacholine test) was added to the definition of asthma, the figures for prevalence were 4.7% in Albacete, 3.5% in Barcelona, 1.1% in Galdácano, 1% in Huelva and 1.7% in Oviedo [3]. In the IBEREPOC study [4] which analyzed the Spanish population between 40 and 69 years of age, 4.9% of the sample reported having been diagnosed with asthma, with the prevalence being greater among women.

The aim of the *Alergológica*-2005 study was to collect information on the current clinical practice in patients consulting an allergologist for the first time as well as to identify the changes that have occurred in the last decade thus replicating the main objectives of *Alergológica*-1995 [5]. This article analyses the changes in the prevalence of asthma and in other clinical and demographic data from the patients suffering from this illness and also the diverse aspects related to the health care and treatment received by these patients.

Materials and Methods

A cross-sectional descriptive, observational, study with prospective collection of data on 4991 patients treated for the first time in Allergology services all over Spain between March 2005 and February 2006 was carried out.

The characteristics of the study and the statistical analysis undertaken are presented in the article on methodology. Briefly, the prevalence of the different allergic disorders was estimated and the remaining qualitative variables were described by calculating relative frequencies (%). Quantitative variables were described by calculating means and standard deviations (SD), using the median as an estimator. Differences between the percentages of quantitative variables were analyzed using the chi-square test. Comparisons between the average values for quantitative variables were made using the student t test. A value of P < .05 was considered to be statistically significant.

Results

Prevalence and Demographic Data

A total of 1396 patients in the sample had bronchial asthma (28%). As in *Alergológica*-1995 [5], asthma represented the second most frequently studied disorder in the Alergología consultations, after rhinitis/conjunctivitis, which was clearly the most prevalent illness (54.7%).

The average age of the patients with asthma was 27 years, with a range of 1 to 86 and a SD of 16.7. Those affected were predominantly children between 5 and 15 years of age and young adults with a clear reduction in frequency in individuals older than 45 years, which probably explained the notable predominance of (extrinsic) allergic asthma which as we shall see, exists in the target population. As for gender, 55.4% were female and 44.6% were male, figures which practically reverse the trend noted in *Alergológica*-1995. In the study population there was a clear predominance of Caucasian subjects (95%) but also a considerable percentage of south American individuals (3.2%). Most patients resided in urban (63%) or semi-urban

(17.8%) areas and only 19% lived in rural areas. Two thirds of patients lived in blocks of flats as opposed to one third who lived in individual houses and the great majority (90%) lived on a level higher than the first floor. The average number of people living in each home was 4. The atmosphere of the homes was considered "dry" by 80% and "damp" by the remaining 20%. Three quarters of the dwellings had central heating (mainly gas or electric) and 38% had air-conditioning.

As for the occupations of the patients, 40.1% were students, 38.7% had non-contaminating jobs, 10% had contaminating jobs, 8.9% did housework and 2.3% were unemployed. Of the child population with asthma, 60.8% attended a kindergarten. Socioeconomic status was middle-to-low in 48.4% of cases, middle-to-high in 44.8%, low in 3.9% and high in 3%.

46.6% of asthmatic patients reported having animals in the home or having frequent contact with animals, mainly pets (90% of cases) and domestic animals the remaining 10%. 3.2% of patients had a stable, generally a building separate from the house. The pets patients had were, in order of frequency, dogs 25.8%, cats 15.2%, birds 9.9%, horses 5.3% rodents 3.5% (of these 49.4% were hamsters, 36.8% rabbits, 12.6% guinea pigs and 1.15% gerbils). Less frequent was the exposure to domestic birds (2.9%), pigs (1.2%), cows (1.1%), sheep (1.1%) and goats (0.7%). In the previous *Alergológica* study [5], 41% of asthmatic patients reported living with animals of which 96% were domestic animals.

The majority of patients were non-smokers (70.3%), 10.4% were ex-smokers and only 14.4% were active smokers.

Clinical and Health Care Aspects

Presenting Complaint

The main presenting complaints of the patients diagnosed with asthma are shown in Table 1. Among the symptoms of asthma, dyspnea appears to be the most frequent manifestation followed by cough and wheezing. Interestingly, a high number of patients also consulted for nasal and eye symptoms.

In 89% of cases patients consulted due to the worsening of previous problems and only in 11% of cases after having suffered the first episode. When examined, most patients were stable (52%) or asymptomatic (15%) and only one third of patients were in an acute phase.

Table 1. Presenting Complaints of Patients Diagnosed with Asthma

Presenting Complaint	%
Dyspnea	77.7
Nasal symptoms	67.2
Cough	64.7
Wheezing	51.8
Eye complaints	46.3
Throat complaints	9.1
Skin problems	7.4
Ear symptoms	4.4
Reactions to drugs	3.7
Reactions to foods	3.7
Elevated total IgE	2.6
Elevated specific IgE	1.7
Infections	1.4

16 S Quirce

History of Atopy

42.2% of patients reported having a first degree relative with asthma, 36.3% with rhinitis, 14.4% with conjunctivitis and 6.7% with atopic dermatitis. As for family history, 32.3% reported having previously been diagnosed with asthma, 32.7% with rhinitis, 15.6% with conjunctivitis, 12.5% with atopic dermatitis and 4% with food allergies.

Asthmatic patients were mainly studied in general practices (45.7%), followed by hospital facilities (32%) and a low percentage (5.6%) of patients were seen in private practices. Half of the patients had been referred from primary care and a quarter were sent by other specialists. The specialists most frequently referring patients to Allergology services were pediatricians (56.6%), followed by specialists in respiratory care (21.3%) and ENT (11.8%) and finally specialists in internal medicine (2.2%). 27.6% of asthmatic patients were evaluated in pediatric allergology services and the remaining 72.4% in adult allergology services.

The mean time between the request for the consultation and completion of the same was 72.4 days, with a median of 30 days.

Onset of the Asthmatic Symptoms and Duration of the Illness

The season in which the asthma symptoms appeared was predominantly the spring (44.1%), followed by autumn (29.4%), winter (21.1%) and summer (5.4%). As can be expected, this predominance of spring can be explained by the high levels of sensitization to pollens in the asthmatic patients studied. As for autumn, the second most frequent season, it is well known that this is a favorable period for the proliferation of dust mites and the subsequent increase in the environmental load of allergens caused by them.

The average duration of the disease was 29.7 months (SD 24.59), that is, approximately two and a half years. However, in 374 cases the duration was greater than 10 years. Given the way in which the question was posed, it was not possible to provide exact data on the average duration of asthma in the full sample.

Suspected Diagnosis

Based only on the clinical history and examination, the diagnosis of asthma was suspected in 95.5% of the patients who were finally diagnosed as suffering from this illness, which indicates the great usefulness of the clinical history when it is properly focused. The high percentage of patients with allergic asthma may have facilitated a correct suspected diagnosis.

Use of Health Care Resources and Worsening of Symptoms

Sixty-nine percent of patients had visited their family doctor due to allergic problems in the 4 months prior to the consultation. Table 2 shows the percentage of patients who had needed to use healthcare services in the 12 months prior to the consultation with the allergologist.

Although the previous questions referred to "allergic disease" in general and were not specific to asthma, it can

Table 2. Use of Healthcare Services in Previous 12 Months

Healthcare Service Use	%
Has attended the Emergency Department in the last year due to allergies	35.8
Has consulted a specialist in the last year due to allergies	28.4
Has been admitted to hospital in the last year due to allergies	4.2
Has been off work in the last year due to allergies	8.3
Has been admitted to hospital in the last year due to other illnesses	4.6
Average number of days of school in the last year in students	11.4

be considered that, given that asthma is one of the allergic diseases that leads to greatest morbidity, a large part of the use of healthcare resources and absenteeism from work was due to asthma. In the present study, to the question of how many times patients had experienced worsening of symptoms over the preceding year, the answer was on average 3.5 times per patient per year, with the median of 2 times. However, in the questionnaire, no clear definition was given of how to understand "worsening of asthma symptoms" and so it was not possible to interpret precisely what kind of symptoms patients were referring to.

Severity of the Asthma

The classification of the "intensity" of the asthma in the opinion of the allergists participating in the study, even though no details were given in the questionnaire as to what criteria to apply to evaluate severity, was mild (57.4%), moderate (40.9%), and severe (1.7%). Furthermore and independently, the "frequency" of the illness also had to be calculated using a dichotomous variable: *intermittent* or *persistent* as a result of which 62.5% of patients were found to have intermittent asthma and 37.5% persistent asthma.

This question was formulated in such a way that it did not follow exactly the classification established in the Global Initiative for Asthma [6] and Spanish Guide for the Management of Asthma [7] guidelines of mild intermittent, mild persistent, moderate persistent and severe persistent. Although the interpretation of the severity of the asthma in these patients must thus be made with caution, all the data point to a clear predominance of patients with mild and moderate asthma.

Quality of Life

The standard version of the SF-12 questionnaire on general quality of life was administered and provided valid results for analysis in 30% of the patients with asthma. The average score for the "physical" component was 44 (SD 9.55) with a range between 16.56 and 66.05. This value is in the 20th percentile of the values of the questionnaire in the general Spanish population which would seem to indicate that the "physical"

aspects of quality of life perceived by asthmatic patients in this study is lower than that of 80% of the Spanish population in general. With regard to the summary of the "mental" scale, the average score was 45 (SD 12.43) with a range between 9.36 and 67.39. This average value corresponds to the 25th percentile for the general Spanish population and so the "mental" aspects quality of life perceived by these patients is lower than that of 75% of the Spanish population in general.

These results confirm previous studies which found that asthma was perceived to have a great impact on the overall health of sufferers, both on the physical and mental aspects [8, 9]. However, it must be borne in mind that the best way of measuring quality of life in asthma is by means of a questionnaire specifically designed to evaluate quality of life for this illness [10].

Diagnosis

Table 3 shows the main diagnostic tests used in consultations in Allergology services to study patients suspected of having asthma. The time used to perform the diagnostic tests was 16 days on average, with a median of 6.5 days.

The most widely used diagnostic tests were, as could be expected, the clinical history, skin tests of immediate hypersensitivity, which were performed in practically all patients. Great use was also made of spirometry (73%) and this figure would have been even higher if children under the age of 6 were excluded.

Etiology of Asthma

Following the classification of Rackeman of bronchial asthma into extrinsic and intrinsic [11], although it would

Table 3. Diagnostic Tests Used

	% of total
Clinical history and examination	98.4
Type 1 skin tests (prick tests)	92.8
Spirometry	73.1
Specific IgE	49.2
Total IgE	47.7
Bronchodilator test	43.3
Blood tests	40.3
Chest X-ray	37.4
Bronchial challenge (metacholine/histamine)	6.6
Alpha 1-antitrypsin	3.8
IgG subclasses	3.0
Ions in sweat	2.7
Local challenge tests (nasal/conjunctival)	2.5
Tuberculin test	2.5
Exhaled nitric oxide	1.9
Eosinophil cation protein	1.9
Exercise test	1.6
Secretory IgA	1.6
Sputum cytology	1.5
Other diagnostic tests*	4,9

Abbreviatures: * Other diagnostic tests include: gasometry, CAT scan of the chest, sputum culture, bronchial challenge with allergens, challenge with drugs, pulmonary diffusion, ECG, reflux studies, delayed tests of hypersensitivity, induced sputum, plethysmography, exhaled breath condensate, challenge with foods and analysis of lymphocyte populations (none of which individually reached 1%).

currently be preferable to use the terms "allergic" and "non-allergic" asthma [12], 1073 patients (79.8%) were diagnosed with extrinsic asthma and 251 (18.7%) with intrinsic asthma and 1.2% with occupational asthma. These percentages are practically identical to those found in the first Alergológica study (81% y 19%, respectively). Among the patients with extrinsic asthma, 52.6% were female whilst among the patients with intrinsic asthma the percentage of females was 65.4% (P<0.001). The patients with intrinsic asthma had a more severe asthma than those patients with extrinsic asthma (P<0.0001).

As for the aeroallergens to which the patients with extrinsic asthma were sensitized, first place was occupied by the pollens 43.8%, followed closely by dust mites (41.4%), and to a lesser extent, animal epithelia (19.6%), fungi (8.4%), food (0.6%), insects (0.2%) and other aeroallergens (1.1%).

The prevalence of sensitization to pollens is practically 10% higher in *Alergológica*-2005 as compared with *Alergológica*-1995, which is a similar figure to the reduction seen in the sensitization to dust mites.

The prevalence of sensitization to allergens from animal epithelia, which was about 20%, is higher than the 15% observed in the previous *Alergológica* study. Both the increase in the prevalence of sensitization to pollens and epithelia seem to confirm the general impression that the atopic diseases caused by these aeroallergens have increased.

Diagnosis of the etiological agent involved in the respiratory symptoms of the patient coincided with the patient's own supposition in a very high percentage of cases – 78.3% - far higher than the 34% agreement in the first *Alergológica* study. This greater degree of recognition of the allergens involved may be related to the greater prevalence of sensitization to pollens and animal epithelia whose involvement in the respiratory symptoms of the patients is easier to identify for obvious reasons. In fact, the reply to the question on the seasonality of asthma, which was affirmative in 43.7% of the total asthmatic population, is practically identical to the percentage of asthmatics with sensitization to pollens.

Apart from the previous section, which asked general questions about the etiology of asthma, a further question was asked about the common aeroallergens which were considered clinically relevant in the patient's asthma. The results, expressed as a percentage of positive replies out of the total number of patients with asthma, are shown in Table 4.

These overall figures of sensitization to aeroallergens must be completed with the detailed data on sensitizations by geographical region, given the great variability which is seen according to where the patient actually lives. This analysis reveals two clear patterns of sensitization. In all the costal areas of the peninsular and in the islands sensitization to dust mites predominates whilst in the inland areas sensitization to pollens predominates. In some regions, such as Andalusia and Navarra, due to their particular geographical and climatic situation, a mixed pattern can be seen with high percentages of sensitization to both pollens and dust mites. Sensitization to animal epithelia (dogs and cats) is particularly high in Madrid, La Rioja and the Canary Islands, and to fungi in Murcia, the Valencian region, Extremadura and Castilla La Mancha.

Of the asthmatic patients sensitized to some animal

18 S Quirce

Table 4. Positive Responses to Aeroallergens in Patients with Asthma (%)

Mites	
Dermatophagoides pteronyssinus	41.0
Dermatophagoides farinae	32.9
Lepidoglyphus destructor	7.7
Tyrophagus putrescentiae Euroglyphus maynei	5.6 3.5
Blomia tropicalis	3.3
Glycyphagus domesticus	1.9
Acarus siro	1.3
Chortoglyphus arcuatus	0.9
Cockroaches	
Blatela spp.	1
Fungi	
Alternaria alternata	8.3
Aspergillus spp. Cladosporium spp.	1.4 1.4
Penicillium spp.	0.4
Others	0.2
Pollens	
Gramineae	32.4
Olea europaea	26.9
Chenopodium album	8.7
Cupressus spp.	7.5 6.9
Platanus acerifolia Plantago lanceolata	6.8
Salsola kali	6.5
Artemisia vulgaris	6.2
Parietaria judaica	4.6
Others*	4.8
* Others include: Betula, Mercurialis, Palmera	
Animal Epithelia	
Cat	15.3
Dog Horse	13.7 2.0
Others*	2.0
* Others include: rabbit, hamster, feathers and co	
, ,	

epithelia (22% of the total), 63% lived with animals (in 90% of cases domestic animals). The animals most frequently owned by these patients were: 37.1% dogs, 27% cats, 9.8% birds, 5.5% rodents and 2% horses.

The percentage of patients with occupational asthma was very low. Only 16 patients (1.2%) of the total, had asthma related to their work, a level of prevalence notably lower than the 4% seen in the first *Alergológica*. study. The substances triggering occupational asthma, expressed as a percentage of the total number of cases of asthma, were foods 0.4%, flours 0.2%, latex 0.2%, isocyanates 0.1%, other chemical substances 0.2%, woods 0.1% and microorganisms 0.1%.

Diseases or Situations Associated with Asthma

Replies to the question on the possible association of asthma with different diseases, special situations and certain triggers (emotions, exercise, laughter) are shown in Table 5. In the present study, rhinitis was more commonly associated with extrinsic asthma (39.5%) than with extrinsic asthma (29.9%), a difference which was statistically significant (P<0.01). As could be expected, in patients with intrinsic asthma the

prevalence of nasal polyposis (10.8%), sinusitis (8.8%) and idiosyncratic reactions to nonsteroidal anti-inflammatory drugs (NSAIDs) was higher than that observed in patients with extrinsic asthma (polyposis 0.9%, sinusitis 2.7% and idiosyncratic reactions to NSAIDs 0.4%, respectively). In all cases these differences were statistically significant (P<.001).

Treatment and Compliance

To the question of whether patients with asthma had received any type of antiallergic treatment in the previous year, 89.7% reported that they had. The treatments they received are shown in the left-hand column of Table 6, expressed as the number of patients with each treatment as a percentage of the total number of patients. Once the allergy analyses had been carried out and the definitive diagnosis of asthma established, the treatment guidelines were those shown in the right-hand column of the Table. Overall, the allergists made at least two changes with regard to the treatments initially prescribed by the non-specialist physicians in 57% of patients. The most significant changes implemented by the allergists were in particular, the introduction of allergy avoidance measures into the treatment regime, the almost two-fold increase in the

Table 5. Comorbidities and Triggers Associated with Asthma*

	% of the total
Rhinitis	36.7
Respiratory infections	25.1
Exercise/laughing	18.1
Worsening of symptoms at night	6.8
Sinusitis	3.7
Atopic dermatitis	3.5
Emotions	2.9
Nasal polyposis	2.7
Pollution	2.7
Idiosyncratic reactions to NSAIDs	1.3
Gastroesophageal reflux	1.2
Others	3.5

Abbreviatures: * NSAIDs indicates nonsteroidal anti-inflammatory drugs.

use of inhalers with a combination of inhaled corticosteroids and long-acting β agonists, an increase in the prescription of antileukotrienes (which also more than doubled) and the prescription of specific immunotherapy which affected 30% of patients.

The frequency of use of the combination of inhaled corticosteroids and long-acting β agonists (38.5%) was somewhat higher than that used in asthmatics treated in hospital pneumology services (49.5%) and higher than that observed in primary care (32%). This probably reflects in part differences in the populations treated by different healthcare providers (age, severity of the illness, etiology, and so on).

As for the differences in therapeutic regimes for asthma between the two *Alergológica* studies, what is particularly striking is the decrease in the use of immunotherapy with

Table 6. Asthma Treatment Received by Patients*

Treatment Avoidance of the allergen (written) 0 71.1 Modification to diet 0 2.8 Change in job or occupation 0 0.5 Inhaled bronchodilators 67.9 78.1 Short-acting 55.7 72.3 Long-acting 8.1 13.8 Systemic bronchodilators 1.7 0.3 Theophyllines ND 0.4 Inhaled corticosteroids 32.5 31.7 Systemic corticosteroids 9 2.3 Corticosteroids + long-acting β-2 Agonists 20.5 38.5 Anti-degranulants 3 1.4 Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/β Agonists ND 0.4 Antileukotrienes 10.3 24.4 Others ND 2.7		Total Number of Patients Before the Consultation With the Allergologist (%)	Total Number of Patients After the Consultation With the Allergologist (%)		
(written) 0 71.1 Modification to diet 0 2.8 Change in job or occupation 0 0.5 Inhaled bronchodilators 67.9 78.1 Short-acting 55.7 72.3 Long-acting 8.1 13.8 Systemic bronchodilators 1.7 0.3 Theophyllines ND 0.4 Inhaled corticosteroids 32.5 31.7 Systemic corticosteroids 9 2.3 Corticosteroids + long-acting β-2 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy Subcutaneous Subcitaneous Subcitaneous Sublingual 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/ β Agonists ND 0.4 Antileukotrienes 10.3 24.4					
Change in job or occupation 0 0.5 Inhaled bronchodilators 67.9 78.1 Short-acting 55.7 72.3 Long-acting 8.1 13.8 Systemic bronchodilators 1.7 0.3 Theophyllines ND 0.4 Inhaled corticosteroids 32.5 31.7 Systemic corticosteroids 9 2.3 Corticosteroids + long-acting β-2 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy Subcutaneous Sublingual 4.4 30.0 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/β Agonists ND 0.4 Antileukotrienes 10.3 24.4		0	71.1		
Inhaled bronchodilators Short-acting Short-acting Short-acting St. Long-acting St. Long-acting St. Systemic bronchodilators Systemic bronchodilators Systemic bronchodilators Systemic bronchodilators Systemic corticosteroids Syste	Modification to diet	0	2.8		
Short-acting Long-acting 55.7 72.3 13.8 Long-acting 8.1 13.8 Systemic bronchodilators 1.7 0.3 Theophyllines ND 0.4 Inhaled corticosteroids 32.5 31.7 Systemic corticosteroids 9 2.3 Corticosteroids + long-acting β-2 Agonists 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/ β Agonists ND 0.4 Antileukotrienes 10.3 24.4	Change in job or occupation	0	0.5		
Long-acting 8.1 13.8 Systemic bronchodilators 1.7 0.3 Theophyllines ND 0.4 Inhaled corticosteroids 32.5 31.7 Systemic corticosteroids 9 2.3 Corticosteroids + long-acting β-2 Agonists 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/β Agonists ND 0.4 Antileukotrienes 10.3 24.4	Inhaled bronchodilators	67.9	78.1		
Systemic bronchodilators 1.7 0.3 Theophyllines ND 0.4 Inhaled corticosteroids 32.5 31.7 Systemic corticosteroids 9 2.3 Corticosteroids + long-acting β-2 Agonists 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/β Agonists ND 0.4 Antileukotrienes 10.3 24.4	e				
Theophyllines ND 0.4 Inhaled corticosteroids 32.5 31.7 Systemic corticosteroids 9 2.3 Corticosteroids + long-acting β-2 Agonists 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/β Agonists ND 0.4 Antileukotrienes 10.3 24.4	Long-acting	8.1	13.8		
Inhaled corticosteroids32.531.7Systemic corticosteroids92.3Corticosteroids + long-acting β-2 Agonists20.538.5Anti-degranulants31.4Antihistamines60.129.8Antibiotic therapy01.6Specific immunotherapy Subcutaneous Sublingual4.430.0Sublingual1.25.1Ipratropium/TiotropiumND1.3Combinations of ipratropium/ $β$ AgonistsND0.4Antileukotrienes10.324.4	Systemic bronchodilators	1.7	0.3		
Systemic corticosteroids 9 2.3 Corticosteroids + long-acting β-2 Agonists 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/ β Agonists ND 0.4 Antileukotrienes 10.3 24.4	Theophyllines	ND	0.4		
Corticosteroids + long-acting β-2 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/β Agonists ND 0.4 Antileukotrienes 10.3 24.4	Inhaled corticosteroids	32.5	31.7		
Agonists 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/B Agonists ND 0.4 Antileukotrienes 10.3 24.4	Systemic corticosteroids	9	2.3		
Agonists 20.5 38.5 Anti-degranulants 3 1.4 Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/B Agonists ND 0.4 Antileukotrienes 10.3 24.4	Corticosteroids + long-acting	Corticosteroids + long-acting β-2			
Antihistamines 60.1 29.8 Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/β Agonists ND 0.4 Antileukotrienes 10.3 24.4			38.5		
Antibiotic therapy 0 1.6 Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/B Agonists ND 0.4 Antileukotrienes 10.3 24.4	Anti-degranulants	3	1.4		
Specific immunotherapy 4.4 30.0 Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/β Agonists ND 0.4 Antileukotrienes 10.3 24.4	Antihistamines	60.1	29.8		
Subcutaneous 3 24.7 Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/B Agonists ND 0.4 Antileukotrienes 10.3 24.4	Antibiotic therapy	0	1.6		
Sublingual 1.2 5.1 Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/ ß Agonists ND 0.4 Antileukotrienes 10.3 24.4	Specific immunotherapy	4.4	30.0		
Ipratropium/Tiotropium ND 1.3 Combinations of ipratropium/ ß Agonists ND 0.4 Antileukotrienes 10.3 24.4	Subcutaneous	3	24.7		
Combinations of ipratropium/ B Agonists ND 0.4 Antileukotrienes 10.3 24.4	Sublingual	1.2	5.1		
β AgonistsND0.4Antileukotrienes10.324.4	Ipratropium/Tiotropium	ND	1.3		
Antileukotrienes 10.3 24.4		ND	0.4		
	ß Agonists	ND	0.4		
Others ND 2.7	Antileukotrienes	10.3	24.4		
	Others	ND	2.7		

Abbreviatures: ND indicates no data available.

allergens (54% to 39%), the prescription of theophylline (26% to 0.4%), and of chromones/ketotifen (53% to 1.4%) as well as the less marked decrease in inhaled corticosteroids from 40% to 31.7%. In contrast, combinations of inhaled corticosteroids and long-acting $\beta\text{-}2$ agonists and antileukotrienes, both of which were absent in the first phase of the study, made a great impact in this second phase of the study with figures of 38.5% and 24.4% respectively.

One important aspect of the treatment of asthma is patient compliance. When asked about the degree of compliance to previous treatment in patients diagnosed with asthma, two thirds of respondents reported compliance to be good, 24% that it was normal while less than 4% acknowledged complying poorly with treatment.

Discussion

The overall prevalence of asthma in the study population was 28%, which represents a notable decrease with respect to the prevalence of 35% observed in *Alergológica*-1995 [5]. It must be highlighted that the data on the prevalence of asthma shown in this study correspond to patients attending an Allergology consultation and therefore the expected levels of asthma frequency are much greater than those observed in the general population.

The percentage of patients undergoing spirometry in this study is similar to the 80% evaluated with this technique among adult asthmatics treated in hospital Pneumology departments [13] and higher than the 50% in asthmatics treated in primary care [9] and much higher than the 36.8% undergoing this test in asthmatics from the general population as studied in the Asthma Insights and Reality in Europe (AIRE) study [14]. All these data refer to Spain. Of interest is also the frequency of use of non-specific bronchial challenge tests (7%), which logically are performed in patients who are more difficult to diagnose. Determination of exhaled nitric oxide was used in 2% of cases. Data on worsening of symptoms and use of healthcare resources are similar to those from the AIRE study [14] carried out in 1999 in 7 European countries, including Spain, where 36% of children with asthma and 28% of adults were found to have received emergency treatment in the previous year. Seven percent of asthmatics in this study had been hospitalized in the previous year.

It is noteworthy that the association with rhinitis, which is the most frequently cited association was not very high – only 36.7%- which is open contradiction with previous epidemiologic studies which have found a frequency of association of between 70% to 90% [15-17]. Such differences may be due to specific biases in the studies, and above all, the methodology used for the diagnosis of the rhinitis and asthma. In this regard, it is probable that the current questionnaire may suffer from methodological shortcomings as 67% of the patients who in fact were diagnosed with asthma experienced nasal symptoms as is shown in Table 1.

After rhinitis, the disorder most frequently associated with asthma were respiratory infections. This association has been previously demonstrated in epidemiologic studies using reliable diagnostic techniques. Indeed, as has been shown by a recent exhaustive review [18], most exacerbations of asthma, especially in children but also in adults, coincide with viral respiratory infections, in particular from rhinovirus. Exercise and laughing (which were not separated in the questionnaire used) also appeared to be frequently associated with asthma attacks (18%). This probably reflects an inadequate control of the illness although worsening of asthma symptoms during the night was experienced by a far lower number of patients (6.8%).

The observed prevalence of nasal polyposis (2.7%) and idiosyncratic reactions to NSAIDs (1.3%) were for the total of asthmatic patients in the lower part of the range, even below the figures usually reported. However, perhaps this finding should not be surprising in a sample of asthmatic patients in which there is a clear predominance of allergic asthma. Using clinical criteria, Giraldo et al [19] found idiosyncratic reactions to NSAIDs in 3% of asthmatics. McDonald et al [20] estimated

20 S Quirce

the prevalence of the phenomenon in asthmatics to be between 10% and 16%. Chafee y Settipane [21], in a study carried out in patients attending an Allergology consultation, found that 4.3% of the asthmatics did not tolerate aspirin when the diagnosis was established using clinical criteria, a figure which rose to 6.8% when oral challenge was used. Castillo y Picado [22] studied the prevalence of aspirin intolerance in asthmatic in-patients and out-patients and found a prevalence of 16% using clinical criteria and 19% with oral challenge.

A low percentage of occupational asthma was observed. This contrasts with published data which indicate that around 10% to 15% of all asthma cases are work-related in origin [23], and also with the European Community Respiratory Health Study data [24] which gave the proportion of cases of asthma in young adults due to work as between 5% and 10%. In the subgroup of Spanish patients in this same study, the risk of asthma attributable to exposure at work was between 5% and 6.7% [25]. However, it must be borne in mind that the epidemiologic studies carried out in the general population do not distinguish between asthma induced by exposure at work (real occupational asthma) and asthma aggravated at work as both categories are included under the more general term "work-related asthma".

The cases described by allergists in the present study probably correspond to patients with a well documented history of occupational asthma and not to cases of asthma aggravated by work conditions. However, the triggering agents which appear in this study are those which are most frequently described in Spain: foods, flours and latex followed by isocyanates and other chemical substances [26].

References

- Janson C, Anto J, Burney P, Chinn S, de Marco R, Heinrich J, Jarvis D, Kuenzli N, Leynaert B, Luczynska C, Neukirch F, Svanes C, Sunyer J, Wjst M. The European Community Respiratory Health Survey: what are the main results so far? European Community Respiratory Health Survey II. Eur Respir J. 2001;18:598-611.
- 2. Grupo Español del Estudio Europeo del Asma. El Estudio Europeo de asma. La prevalencia de síntomas relacionados con el asma en 5 regiones de España. Med Clin (Barc). 1995;104:487-92.
- 3. Grupo Español del Estudio Europeo del Asma. El Estudio Europeo del asma. Prevalencia de hiperreactividad bronquial y asma en jóvenes en 5 regiones España. Med Clin (Barc). 1996;106:761-7.
- Sobradillo V, Miravitlles M, Jiménez CA, Gabriel R, Viejo JL, Masa JF, Fernández-Fau L, Villasante C. Epidemiological study of chronic obstructive pulmonary disease in Spain(IBERPOC): prevalence of chronic respiratory symptoms and airflow limitation. Arch Bronconeumol. 1999;35:159-66.
- Alergológica. Factores epidemiológicos, clínicos y socioeconómicos de las enfermedades alérgicas en España. SEAIC. Editorial Nilo, Madrid 1995.
- 6. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention: NHLBI/WHO workshop report, publication No. 02-3659, 2002.
- 7. Guía Española para el Manejo del Asma (GEMA). Grupo Español para el Manejo del Asma. Ediciones Mayo. Barcelona, 2003.
- 8. Leynaert B, Neukirch C, Liard R, Bousquet J, Neukirch F. Quality of

- life in allergic rhinitis and asthma. A population-based study of young adults. Am J Respir Crit Care Med. 2000;162:1391-6.
- Laforest L, Bousquet J, Pietri G, Sazonov Kocevar V, Yin D, Pacheco Y, Van Ganse E. Quality of life during pollen season in patients with seasonal allergic rhinitis with or without asthma. Int Arch Allergy Immunol. 2005;136:281-6.
- Juniper EF, Buist AS, Cox FM, Ferrie PJ, King DR. Validation of a standardized version of the Asthma Quality of Life Questionnaire. Chest. 1999:115:1265-70.
- Rackeman F. A working classification of asthma. Am J Med. 1947:3:601-6.
- Romanet-Manent S, Charpin D, Magnan A, Lanteaume A, Vervloet D; EGEA Cooperative Group. Allergic vs nonallergic asthma: what makes the difference? Allergy. 2002;57:607-13.
- López-Viña A, Cimas JE, Díaz Sánchez C, Coria G, Vegazo O, Picado Valles C. A comparison of primary care physicians and pneumologists in the management of asthma in Spain: ASES study. Respir Med. 2003;97:872-81.
- 14. Rabe KF, Vermeire PA, Soriano JB, Maier WC. Clinical management of asthma in 1999: the Asthma Insights and Reality in Europe (AIRE) study. Eur Respir J. 2000;16:802-7.
- 15. Pedersen P, Weeke E. Asthma and allergic rhinitis in the same patients. Allergy. 1983;38:25-9.
- Greisner W, Settipane R, Settipane G. Co-existence of asthma and allergic rhinitis: a 23-year follow-up study of college students. Allergy Asthma Proc. 1998;19:185-8.
- Guerra S, Sherrill D, Martinez F, Barbee R. Rhinitis as an independent risk factor for adult-onset asthma. J Allergy Clin Immunol. 2002;109:419-25.
- Johnston NW, Sears MR. Asthma exacerbations. 1. Epidemiology. Thorax. 2006:61:722-8.
- 19. Giraldo B, Blumenthal MN, Spink WW. Aspirin intolerance and asthma. A clinical and immunological study. Ann Intern Med. 1969;71:479-96.
- Mc Donald JR, Mathison DA, Stevenson DD. Aspirin intolerance in asthma. Detection by oral challenge. J Allergy Clin Immunol. 1972:50:198-207.
- 21. Chafee FH, Settipane GA. Aspirin intolerance. I. Frequency in an allergic population. J Allergy Clin Immunol. 1974;53:193-9.
- Castillo JA, Picado C. Prevalence of aspirin intolerance in asthmatics treated in a hospital. Respiration. 1986;50:153-7.
- Blanc P. Occupational asthma in a national disability survey. Chest. 1987;92:613-7.
- Kogevinas M, Antó JM, Sunyer J, Tobias A, Kromhout H, Burney
 P. Occupational asthma in Europe and other industrialised areas: a population-based study. Lancet. 1999;353:1750-4.
- 25. Kogevinas M, Antó JM, Soriano JB, Tobias A, Burney P. The risk of asthma attributable to occupational exposures. A population-based study in Spain. Spanish Group of the European Asthma Study. Am J Respir Crit Care Med. 1996;154:137-43.
- Sastre J, Quirce S. Patología respiratoria alérgica ocupacional. Emisa. Madrid, 2003.

Dr. Santiago Quirce

Allergy Service, Hospital La Paz, P. Castellana, 261, 28046 Madrid, Spain Tel: 91 727 70 80

E-mail: squirce@gmail.com