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Asthma control in Spain. Do season and treatment pattern matter? The ESCASE study

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Summary
The aim of this study was to assess the degree of asthma control according to GINA criteria during two different seasons in Spain.
An multicenter, longitudinal, epidemiological study with the participation of a sample of physicians in Spain was conducted. Consecutive asthma patients, 18 years of age and older, seeking primary and specialist care were included in the study. Patients were seen during the winter and spring 2004 and were asked about asthma control according to GINA control criteria (daytime and nighttime symptoms, asthma exacerbations, limitations of physical activity, and visits to the emergency department) during the 4 weeks prior to the visit. Control was defined according to daytime and nighttime symptoms.
A total of 614 patients participated in the study. The proportion of patients reporting daytime symptoms "every day" or "most days" during the winter versus spring was 40.1% vs. 23% ($P<0.01$); 26.9% vs. 14.1% presented symptoms at night ($P<0.01$); 11.5% vs. 8.3% had severe exacerbations; 33.5% vs. 35.7% presented symptoms accompanying exercise, and 9.4% vs. 4.3% ($P<0.01$) had required emergency visits. The number of patients with inadequate control was slightly higher in winter than in spring (74.4% vs. 71%) ($P<0.01$). The most commonly prescribed treatment was ICS plus LABAs for both periods.

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Asthma is poorly controlled in Spain and strategies are needed to improve management of this illness.

Introduction

Asthma is a chronic disease, common in developed countries, and a progressive increase in asthma has been reported worldwide.[1,2] Given the morbidity and mortality associated with asthma, it is becoming an increasingly serious public health concern.[3,4]

The European Community Respiratory Health Survey (ECRHS), conducted between 1991 and 1993, examined the prevalence of asthma in adults in 22 countries throughout the world including Spain.[5] According to this study, the mean global prevalence of asthma was 4.5% (range 2.0–11.9%)[6,7]; whereas in Spain tremendous geographical variability was observed ranging from 5% in Galdakano to 14.5% in Huelva.[8,9]

In an attempt to improve the quality of healthcare for asthma sufferers, as well as to decrease burden of the disease on public healthcare systems, the International Global Initiative for Asthma (GINA) guidelines and the Spanish National Guidelines for the Management of Asthma (GEMA) have been established.[10,11]

Despite the theoretical consensus surrounding the management of asthma, several studies have shown that the treatment recommendations for asthma published in the guidelines are not always followed as would be expected.[12–16] The Asthma Insights & Reality in Europe (AIRE) Study, a multi-national, population-based telephone survey, showed that 94.7% of all patients fail to achieve proper control of their disease.[12] An office-based study conducted in Spain, the ASES Study, confirmed that the percentage of patients who reported suffering symptoms more than once a week at primary care and pneumologist office visits was 24% and 32%, respectively.[17] Despite these findings, recent data indicate that the use of proper treatment, which would include the combination of a long-acting β_2 agonist and inhaled corticosteroids (ICS) at the required doses and duration, could improve asthma control.[18] Climate changes have been described among asthma precipitating factors[19,20] and may increase the percentage of asthma patients with poor asthma control.

The primary endpoint of this study was to determine the level of asthma control in Spain and to assess the changes in asthma control during two different seasons in Spain—winter and spring. The main study hypothesis is that despite previous studies and guidelines, asthma control in Spain remains limited.

Methods

This is an multicenter, longitudinal, epidemiological study with retrospective data collection. Study participants attended a total of two study visits, one in the winter and the other one in the spring, in order to evaluate the degree of asthma control during each period. According to expert consensus, the distribution among allergists, pneumologists, and primary care physicians was established so as to be representative of the entire Spanish territory and applied per autonomous community. Reliable data are not available regarding the distribution of healthcare services in Spain (primary care, allergology, and pneumology); hence, the decision was made to base the results on an expert consensus panel (approximately 45% primary care, 15% allergology, and 40% pneumology). The study was approved by an Ethics Committee and all the participants signed an informed consent document.

Patients aged 18 years or older with a GINA-based diagnosis of asthma for more than 1 year and no concomitant chronic respiratory disease were consecutively included in the study that contemplated two study visits. The first one in the winter during the first 2 weeks in March, 2004; the same patients were seen again in the spring during the first half of May, 2004.

Sociodemographic data (age, gender, smoking status) and clinical variables (years since asthma diagnosis, allergic and non-allergic asthma, asthma severity, concomitant disease, and asthma therapy) were collected. Allergic asthma was defined by a positive allergy test, independently of IgE levels.

Subjects answered questions about the presence of any of the following GINA control criteria in the preceding 4 weeks: daytime symptoms, nighttime symptoms, asthma exacerbations (defined as severe, sudden episodes of coughing, wheezing, or difficulty breathing), limitations of physical activity, and emergency visits.

An operational definition of asthma control based only on the frequency of daytime and nighttime symptoms according to GINA severity criteria was agreed upon (Table 1) and applied to study patients in the statistical analysis phase.

Table 1 Definition of asthma control based on daytime and nighttime symptoms following GINA clinical severity criteria.

GINA	Operational definition	
Daytime and nighttime symptoms	Asthma control	Asthma control
Intermittent	Good	Good
Mild persistent	Moderate	Inadequate
Moderate persistent	Poor	Inadequate
Severe persistent	Poor	Inadequate

The following categories were defined irrespective of the treatment patients were receiving at the time: "good control", when the severity of symptoms was *intermittent* during the day and at night; "moderate control", when symptom severity was *mild*, and "poor control" when there were *moderate or severe* symptoms during the day and at night. Patients were defined as *controlled* if they presented "good control" of their asthma and as *inadequately controlled* when they had "moderate control" or "poor control". Definition of *intermittent*, *mild*, and *moderate*, or *severe* were defined according to the GINA classification in terms of nighttime and daytime symptoms.

The asthma treatment pattern variable was categorized into the following groups: (1) no therapy; (2) monotherapy: short-acting β_2 adrenergics (SABAs), long-acting β_2 adrenergics (LABAs), ICS, or leukotriene receptor antagonists (LRAs); (3) combined treatment: ICS+LABAs, ICS+LABAs+LRAs, and (4) other regimes that included primarily treatment with theophylline and anticholinergics, or other combinations such as ICS+LRAs and LABAs+LRAs. Immunotherapy and oral corticosteroid use were classified as independent dichotomous variables.

A sample size of 547 patients was calculated in order to be able to estimate that 35% of the asthmatic patients had good asthma control at the follow-up visit with a four-point level of accuracy and significance level of 0.05.[16]

Statistical analysis

Student's *t*-test or χ^2-test was used when appropriate to compare continuous or categorical variables between independent groups. McNemar's test for paired data was used to compare GINA control criteria between seasons.

The SPSS software package (version 10.1.3 for Windows) was used for data analysis. The level of statistical significance was defined as an alpha value <0.05.

Results

Sixty-seven physicians from all over Spain participated in the study: 31 (46%) primary care physicians, 26 (39%) pneumologists, and 10 (15%) allergists. A total of 614 patients were recruited in winter, with an average of eight patients per investigator. A total of six patients in winter and six in spring had not completed the asthma control information and were excluded from the final analysis. Another eight patients were lost to follow-up at the spring visit. A 594-patient sample was finally analyzed. No differences were found upon comparison of patients excluded from the final analysis with non-excluded patients.

Baseline sociodemographic and clinical characteristics are presented in Table 2. Mean patient age was 49.6 years and there was a greater proportion of females versus males (64%). At the time of asthma diagnosis, most patients were non-smokers (63.5%), had a history of asthma of more than 10 years (52.9%), and presented mild and moderate persistent asthma (33% each category). Asthma was allergic in origin in 55.2% of the patients. The most frequently reported concomitant disease was allergic rhinitis (48.7%). At baseline, most patients (50.3%) were on combined asthma therapy consisting of ICS and LABAs.

Table 2 Patient baseline sociodemographic and clinical characteristics.

Baseline characteristics ($n = 594$)	*N* (%)
Age, years (SD)	49.6 (18.1)
Gender, female	380 (64)
Smoking status	
Smoker	66 (11.1)
Ex-smoker	150 (25.3)
Non-smoker	376 (63.5)
History of asthma	
$<$ 5 years	120 (20.3)
5–9 years	158 (26.8)
$>$10 years	312 (52.9)
Type of asthma	
Allergic	326 (55.2)
Non-allergic	211 (35.7)
Unknown	54 (9.1)
Concomitant disease	
Allergic rhinitis	289 (48.7)
Conjunctivitis	149 (25.1)
Dermatitis	74 (12.5)
*Severity of asthma (GINA)**	
Intermittent	141 (23.9)
Mild persistent	199 (33.8)
Moderate persistent	196 (33.3)
Severe persistent	53 (9.0)
Reason for visit	
Regular check-up	408 (69.3)
Increase in symptoms	65 (11)
Need for medication	58 (9.8)
Other	58 (9.8)
Asthma treatment	
No therapy	7 (1.2)
Monotherapy	193 (32.5)
SABA	59 (9.9)
ICS	91 (15.3)
LABA	34 (5.7)
LRA	9 (1.5)
Combined therapy	372 (62.6)
ICS+LABA	299 (50.3)
ICS+LABA+LRA	73 (12.3)
Other regimens†	22 (3.7)
Oral corticosteroids	33 (5.6)
Immunotherapy	13 (2.2)

Missing data: smoking status (2), history of asthma (4), type of asthma (3), concomitant disease (1), asthma severity (5), and reason for visit (5).

*At the time of diagnosis.

†Other regimens included: theophylline (5), anticholinergics (5), or other atypical combinations such as ICS+LRAs (11) and LABAs+LRAs (1).

Asthma control according to season

Patients' responses to five GINA control criteria corresponding to the 4 weeks prior to the visit for the two seasons are shown in Table 3. Daytime or nighttime symptoms, asthma exacerbations, limitations of physical activity, and emergency visits. The most frequently reported symptoms in winter and spring were daytime symptoms and limitations of physical activity. Statistically significant differences in the percentage of patients with some degree of symptoms between periods were not detected. "Every day" or "most days" daytime and nighttime symptoms were significantly higher in winter than in spring (40.1% vs. 23% and 26.9% vs. 14.1%, respectively), whereas no seasonal differences were found for limitations of physical activity "every day" or "most days" (33.5% vs. 35.7%, respectively). Although the proportion of patients reporting asthma exacerbations "every day" or "most days" was higher in winter, the differences between seasons were not statistically significant (11.5% vs. 8.3%, respectively). The proportion of patients requiring visits to the emergency room at anytime was significantly higher in winter than in spring, 9.4% vs. 4.3%, respectively. When any symptom frequency is taken into account (first and third column of Table 3), the proportion of patients with symptoms is consistently greater in winter.

The percentages of patients defined as having a good control, moderate control, and poor control are shown in Fig. 1. A slightly larger proportion of patients presented inadequate control (moderate or poor) in the winter compared to the spring, 74.4% vs. 71%, respectively ($P<0.01$). The proportion of patients reporting poor control significantly decreased in the spring, 34.7% vs. 21%, respectively ($P<0.05$).

In 15.8% of the patients, the asthma treatment pattern had been modified in the interval between both study visits. Given the huge diversity of prescribed treatments, the percentage of patients in whom treatment had been changed was not analyzed because the figures for each group would have been too low to achieve significance.

Asthma control-related variables

Bivariate analysis revealed that relations between asthma control and sociodemographic (age and gender), clinical (history of asthma, type of asthma, and asthma severity) or smoking status variables lacked statistical significance. Asthma control was only seen to be related to the presence

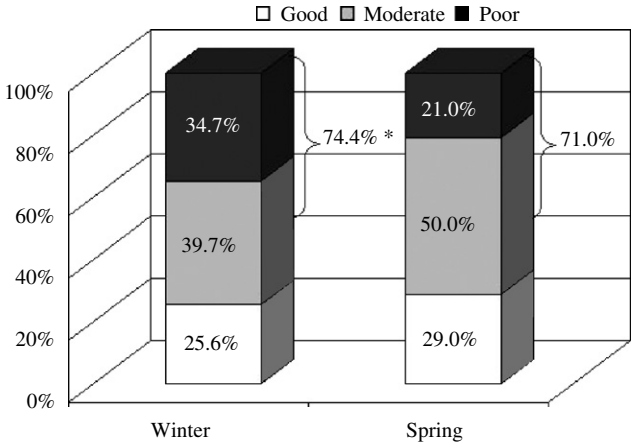

Figure 1 Asthma control in Spain according to frequency of daytime and nighttime symptoms in two seasonal periods. Control was defined based on daytime and nighttime symptoms according to GINA severity criteria: good = intermittent asthma; moderate = mild persistent asthma; poor = moderate to severe persistent asthma.*$P<0.01$.

Table 3 Asthma control over the 4 weeks preceding study visits according to GINA criteria.

Symptoms	Winter		Spring	
	% with symptoms*	% high frequency†	% with symptoms*	% high frequency†
How often have you had symptoms during the day?	70.9	40.1	67.2	23.0‡
How often have you had symptoms at night?	47.5	26.9	44.5	14.1‡
How often have you had a severe asthma attack/ exacerbation?	25.1	11.5	20.9	8.3
How often have you suffered from any symptom during physical activity?	69.2	33.5	66.0	35.7
How often have you gone to the emergency room for your asthma?	9.4		4.3‡	

*Proportion of study patients describing any symptom frequency or with at least one visit to the emergency department.
†Proportion of patients with symptoms "every day" or "most days" calculated over the total number of patients with each symptom (positive response in previous column).
‡$P<0.01$.

of certain specific diseases such as depression ($P<0.01$), diabetes ($P<0.01$), or cardiovascular diseases ($P<0.05$), and to the reason for the visit ($P<0.01$) and treatment pattern ($P<0.05$).

Discussion

Despite a commonly held view that asthma control can be attained in most patients, different studies have shown that the objectives for good control proposed by international reference guidelines are still far from being met.[12–16]

To our knowledge, this is the first paper that examines asthma control in the Spanish population by personally interviewing a sample of patients who sought care from any of three different medical specialties: primary care physicians, pneumologists, and allergists. Given that these patients were seen periodically by clinicians, one would have expected to see better disease control than what has been observed in studies such as the AIRE Study, where asthmatic patients participated in a telephone survey of the general population.[12] Nonetheless, our findings confirm a degree of inadequate asthma control similar to that of previous studies.[12–16]

Combining the frequency and severity of daytime and nighttime symptoms in the 4 weeks prior to the visits, only 25.6% of the patients was seen to have good control of their asthma at the winter visit. While these figures improved in the spring, they remained well below the recommended levels of control. By interviewing the same patients on two different occasions, the intervention itself may have improved the outcomes; thus, these results should be interpreted with caution. However, should this supposition be true, it would be worth hypothesizing as to what educational, reminder, or self-monitoring interventions might be carried out that could enhance control of this illness.

Other studies have assessed asthma control in different settings. In the AIRE Study, subjects were randomly selected from the general population by means of a telephone survey and asthma control was defined as meeting GINA criteria for "good control", "moderate control", and "poor control", depending on whether 0–1, 2–3, or 4–5 of the GINA criteria were met, respectively.[12] Of the 2050 adults with asthma who finally participated in the study, 35% of the cases were seen to have "good" disease control; 40% had "moderate" control, and in the remaining 25%, control was "poor". In the ASES Study comparing asthma management by pneumologists with primary healthcare physicians in Spain, López-Viña et al.[17] found that more than 25% of the participants reported nighttime symptoms on more than two occasions per month and 24% had visited the emergency room in the previous year. Despite differences in the definition of control, these data reconfirm the unexpectedly low level of adequate asthma control in different settings.

This study was not designed to examine the reasons for the poor asthma control reported, although previous studies have shown that despite the fairly explicit current treatment guidelines for managing the disease, a high percentage of physicians do not follow the established recommendations.[21] A recent study has demonstrated that when treatment is stepped-up appropriately and maintained for long enough, proper control can be achieved in an important percentage of patients.[22] The fact that some studies have also shown that patients used their medication inappropriately, even when presenting moderate or severe asthma symptoms is of even greater concern.[12–16] Hence, the dual effect of failure to comply with recommendations on the part of the physician and poor patient adherence to treatment might be considered to be the leading cause of poor disease control.[12–16] On the other hand, although recent studies have shown that with appropriate treatment it is possible to reach the objectives purported by the guidelines,[18] neither patients nor physicians are very demanding when it comes to establishing to what extent these objectives should be met and both are willing to believe that some symptoms are simply part of the disease. In a study conducted in the UK, Jones et al.[23] included 1031 asthmatic patients, 51% of whom considered their health status to be good and accepted certain limitations in their daily lives due to their disease as normal. Data compiled by the Spanish group of the European study on asthma showed that more than half of the people with asthma stated either that they did not have or had not had asthma and approximately one-third were not treated for the disease.[8] Another recent study published by Bellamy and Harris[24,25] examined patients' and physicians' opinions regarding the level of disease control and showed that most patients (82%) considered that their asthma was not controlled and most physicians (70%) believed that their patients accepted the symptoms of the disease as normal and were well adapted to their daily routines.

This study has a number of limitations. First, there is the issue regarding sample representativity. Reliable data are not available with respect to the distribution of healthcare areas in Spain; consequently, it was decided to base the results on an expert consensus panel. Nonetheless, a homogeneous office distribution was applied in the different Autonomous Communities despite the fact that there might be geographical differences in terms of healthcare resources. Therefore, the results observed may not be representative of the different geographical regions. Second, lung function was not recorded and asthma severity was recorded retrospectively at the time of diagnosis. It is possible that these criteria were not accurate to define the current severity of illness and this may explain why severity was not associated with disease control. Third, an operational definition was used to define asthma control based on daytime and nighttime symptoms. This definition could have introduced some misclassification leading to either an over- or underestimation of the effect size. Nonetheless, daytime and nighttime symptoms were the two only clinical criteria that showed statistically significant differences between winter and spring. Therefore, we speculate that these two criteria alone are good indicators of asthma control and suggest that using such an easy clinical indicator of control may make it easier to manage asthma in routine, daily practice. Finally, the seasons were selected by convenience and no objective weather parameters such as temperature, humidity, wind, or rainfall were collected; moreover, pollen count data is unavailable. As a result, the interaction between allergens, weather, and asthma control could not be evaluated and hence, it cannot be ruled out that the seasonal changes detected in the study were largely

determined by the study intervention. However, the homogeneous trend towards a higher proportion of patients with symptoms, exacerbations, and emergency room visits during the winter confirms our results.

In summary, the findings of this study show that asthma control in Spain remains very far from the long-term objectives established by GINA. Improving asthma management together with greater patient awareness in complying with medical recommendations are important issues if control of the disease is to be improved.

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