ORIGINAL ARTICLES

Rate and Characteristics of Asthma Exacerbations: The ASMAB I Study

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OBJECTIVE: The aim of this study was to determine the incidence and clinical characteristics of asthma exacerbations seen by emergency services in Barcelona, Spain (the ASMAB-I study).

PATIENTS AND METHODS: The emergency services considered in the study served a population of 1 203 598 inhabitants aged over 14 years. Episodes treated in hospital emergency departments and by emergency services called to patients' homes over a period of 129 days were included in the study.

RESULTS: In total, 831 episodes of exacerbation were identified; 523 were seen in 3 university hospitals, 113 in secondary hospitals, and 195 by emergency services at the patient's home. Twenty of the patients seen at home were subsequently taken to hospital. The mean frequency was 6.4 episodes per day, corresponding to a daily incidence of 0.53 exacerbations per 100 000 inhabitants (95% confidence interval, 0.46-0.56 exacerbations/100 000 inhabitants) and 8.2 per 100 000 asthmatic patients (95% confidence interval, 6.89-8.41 exacerbations/100 000 asthmatic patients). Of the 276 episodes treated between Monday and Thursday in university hospitals, 66 patients (24%) reported acute onset and 14 (5%) sudden onset. Only 85 patients (31%) regularly used inhaled corticosteroids and only 33 (12%) added oral corticosteroids in the 12 hours prior to consulting emergency services. In 16% of cases the episode was classified as severe and in 3% near fatal. Eighty-two patients (30%) were ultimately admitted to hospital: 12% of mild exacerbations, 39% of moderate exacerbations, 62% of severe episodes, and 100% of near-fatal episodes. The Charlson comorbidity index was higher in patients admitted to hospital (*P*<.001). In the 28 patients readmitted to hospital (10%), antibiotics (*P*<.001) and ipratropium bromide (*P*<.0001) had been prescribed less often at the time of discharge after the first hospital admission.

CONCLUSIONS: The rate of asthma exacerbation established in this study may be a useful indicator of the degree of control of the disease and may serve as a reference to confirm future short-term or lasting increases in asthma exacerbation. Rapid onset (acute or sudden) is common and many patients are not receiving appropriate treatment prior to hospital admission. Severe exacerbation is common in our practice setting. Hospital admission is related to severity and comorbidity. Patients who are readmitted to hospital had less often received antibiotic treatment and ipratropium bromide when discharged previously.

Key words: *Asthma exacerbation. Severe asthma exacerbation. Readmission. Comorbidity. Emergency services. Hospital admission. Epidemiology.*

Tasa y características de las agudizaciones asmáticas (ASMAB I)

OBJETIVO: El presente estudio examina la incidencia y las características clínicas de los episodios de agudización asmática (AA) atendidos en los servicios de urgencias (SU) de la ciudad de Barcelona (estudio ASMAB-I).

PACIENTES Y MÉTODOS: Se estudiaron los episodios de AA atendidos en los SU hospitalarios y en el SU domiciliario (061) durante 129 días, correspondientes a una población mayor de 14 años de 1.203.598 habitantes.

RESULTADOS: Se identificaron 831 episodios de AA, de los que 523 fueron atendidos en 3 hospitales universitarios, 113 en 2 hospitales de segundo nivel y otros 195 (de los que 20 se remitieron a hospitales) en los SU domiciliarios. La frecuentación media fue de 6,4 episodios/día, con una incidencia de AA de 0,53/10⁵ habitantes/día (intervalo de confianza del 95%, 0,46-0,56) y de 8,2/10⁵ pacientes asmáticos (intervalo de confianza del 95%, 6,89-8,41). De los 276 episodios atendidos de lunes a jueves en los servicios de los hospitales universitarios, 66 pacientes (24%) reconocieron un inicio agudo y 14 (5%) un inicio súbito. Únicamente 85 pacientes (31%) tomaban de modo regular corticoides inhalados y sólo 33 (12%) añadieron corticoides orales en las 12 h previas a su llegada a urgencias. Un 16% de los episodios se calificaron de graves y un 3% de casi fatales. Un total de 82 pacientes (30%) fueron finalmente hospitalizados; ingresaron el 12% de las AA leves, el 39% de las AA moderadas, el 62% de las AA graves y el 100% de las casi fatales. El índice de comorbilidad de Charlson fue mayor en los pacientes hospitalizados (p < 0,001). En los 28 readmitidos (10%), al darles el alta previa se les habían prescrito menos antibióticos (p < 0,001) y bromuro de ipratropio (p < 0,0001).

CONCLUSIONES: La tasa de AA establecida puede ser un indicador útil del grado de control del asma y servir para confirmar futuros aumentos de AA permanentes o puntuales. El inicio rápido (agudo o súbito) es frecuente. Muchos

pacientes no reciben un tratamiento adecuado antes de la hospitalización. La agudización grave es frecuente en nuestro medio. El ingreso está relacionado con la gravedad y la comorbilidad. Los readmitidos han recibido al alta menos antibióticos y bromuro de ipratropio.

Palabras clave: *Agudizaciones asmáticas. Agudización grave del asma. Readmisiones por asma. Ingresos por asma y comorbilidad. Servicios de urgencias. Hospitalización por asma. Epidemiología del asma.*

Introduction

Bronchial asthma is a common disease,[1] with a prevalence in industrialized countries that reaches between 10% and 13% of the population.[2] In the last 10 years, the prevalence has doubled in Western European countries and 27% of the asthmatic population in those countries are reported to have required treatment for exacerbations in the last year.[2] The need for treatment of exacerbation may be the result of inadequate management of asthma in Europe,[3] as has been reported in the United States.[4] Asthma exacerbations could be an epiphenomenon associated with poor disease control,[5,6] or they could be a response to one or more trigger factors,[7] such as viruses or allergens.[8]

Determining the rate of asthma exacerbation in a population of asthmatic patients could serve as an indicator of deficiencies in chronic therapy or possible poor clinical management of the patients, as well as provide confirmation of the involvement of an environmental trigger. However, identification of all cases of asthma exacerbation occurring in a given population requires enormous collaboration from both patients and their physicians, and as a result, continuous follow-up is impractical. A simpler approach is to analyze asthma exacerbations seen by hospital emergency departments and emergency medical services in a given area.

The identification of outbreaks of asthma due to soy associated with unloading of soybeans in the port of Barcelona,[9,10] in which the frequency of cases seen in hospital emergency departments led to the identification of an increase in asthma exacerbations in the city on certain days, led us to extend our analysis of the incidence of exacerbation in this study by also adding asthma exacerbations seen by out-of-hospital emergency medical services. In addition, in an effort to define the clinical characteristics of these asthma exacerbations in order to act in the future to resolve the problems identified, the secondary objective of the study was to analyze various clinical variables: the characteristics of the patients at onset of asthma exacerbation, the chronic treatment that they were receiving, treatment provided by emergency services, and whether or not treatment had been increased when the exacerbation began, as recommended in international guidelines.[11] It is known that inappropriate prescription or poor treatment adherence can lead to severe exacerbation

of asthma and even death in some patients.[12] Finally, the severity of the episodes was classified and the patient's body mass index (BMI) calculated. Thus, the aim of this study was to analyze the rate of asthma exacerbation seen by emergency services as an indicator of the degree of clinical control of patients' disease and to determine the characteristics of the patients who suffered exacerbations.

Patients and Methods

Study Design

A prospective study was performed to identify episodes of asthma exacerbation in patients aged over 14 years seen in hospital emergency departments and by emergency medical services in an area of Barcelona, Spain. The primary objective of the study was to calculate the incidence of exacerbation occurring each day in asthmatic patients from a section of the population and to relate that incidence to the entire population of the study area. The secondary objective was to describe the clinical characteristics of the episodes of asthma exacerbation treated in emergency departments of tertiary level hospitals by reviewing the medical history of each episode treated and interviewing the patient.

The study was approved by the Institutional Review Board of Hospital Universitari Vall d'Hebron (reference PR(AG) 27/2005).

Identification of Asthma Exacerbations

All episodes of asthma exacerbation occurring in patients over 14 years of age seen in emergency departments of public hospitals or by emergency medical services in an area covering three-quarters of the city of Barcelona were identified for the period from November 1, 2001 to March 9, 2002, a total of 129 days. If a patient had another exacerbation during that period it was counted as a new episode. All patient histories from emergency departments were reviewed for the hospitals in the study area (3 tertiary level and 2 secondary level hospitals) and those classified as asthma-related emergencies and that had been recorded with the following diagnoses were identified: bronchial asthma, bronchospasm, bronchial hyperresponsiveness, asthmatic bronchitis, spastic bronchitis, status asthmaticus, asthma crisis, acute or severe asthma attack, or severe asthma exacerbation. The diagnosis of asthma exacerbation was confirmed for each patient based on review of the medical history from the emergency department by 2 of the authors (T. G. and F. M.) according to the guidelines proposed by the Global Initiative for Asthma (GINA)[13]: history of episodes involving shortness of breath, wheezing, or tightness of the chest, or some combination of those symptoms; a family history of asthma or atopic disease contributed to establishing the diagnosis.

Of the 276 episodes treated in the tertiary level hospitals between Monday and Thursday (period chosen to allow collection of data over the weekend) and for which diagnosis was confirmed following review of the medical history from the emergency department, the diagnosis could be reaffirmed in 128 (following face-to-face interview in 103 and telephone contact in 25). In the 113 episodes treated in secondary level hospitals, the asthma exacerbations were identified by one of the authors of the study based on review of the patient history from the emergency department.

In parallel, all episodes of asthma exacerbation seen outside the hospital by emergency medical services were identified for the study area. A diagnosis of asthma exacerbation was established by the emergency medical specialist who had visited the patient. The episodes seen first by emergency medical services and later

referred to hospital were only counted once. Death certificates issued by the hospital and reports from autopsies performed during that period were also reviewed. Patients in whom autopsy was performed would have been seen at some point in the emergency department, and were therefore only counted once.

Risk Population

According to the census for the city of Barcelona,[14] a total of 449 210 people live in the area served by Hospital Universitario Vall d'Hebron, 285 188 in the health care area of Hospital del Mar, and 625 604 in the area served by Hospital Clínic and the 2 secondary level hospitals (Hospital del Sagrat Cor and Hospital de Barcelona), corresponding to a combined population of 1 360 002 individuals. Individuals aged less than 14 years represented 11.5% of the population (156 404 children); therefore, the study population above 14 years comprised 1 203 598 individuals. The percentage of asthmatic patients in a population aged between 20 and 44 years in Barcelona was estimated at 6.5%,[15] which would correspond to a total of 78 233 patients in our population of individuals aged above 14 years.

Clinical Characteristics and Treatment of Severe Asthma Exacerbations in Tertiary Level Hospitals

Assessment of the clinical characteristics and treatment of severe asthma exacerbations was restricted to patients seen in the 3 tertiary level hospitals. In order to make time available for data collection during the weekends, we only recorded cases treated from Monday through Thursday. As a result, 68 days were analyzed for this part of the study. Data were recorded on standardized forms that included the following information: patient's clinical history, including the day on which the disease worsened and place where this occurred[16]; whether the onset of the exacerbation was acute, that is, occurring in less than 3 hours, or sudden, occurring in less than 30 minutes[17] (we distinguished between these 2 forms, encompassing rapid-onset exacerbation, because the asthma epidemic that occurred in Barcelona between 1981 and 1988 due to inhalation of soybean dust involved sudden-onset exacerbation in many cases); chronic treatment used by the patients[18]; and the medication used in the 12 hours prior to arrival in the emergency department.[19] The severity of the exacerbations was determined according to the criteria adopted in the 2002 GINA report[20]; if the classification was not consistent for all variables, the severity of the episode was classified according to the variable showing the greatest severity. The episode was considered near-fatal or life-threatening when at least 1 of the following criteria was met: *a)* respiratory arrest, *b)* requirement for a ventilator, or *c)* $PaCO_2$ greater than 50 mm Hg.[17] The number of patients admitted to hospital, classified as those who remained in hospital for more than 24 hours, was recorded. The Charlson comorbidity index was calculated for each level of severity.[21]

Interview Following Hospital Discharge

Fifteen days after patients admitted to the 3 tertiary level hospitals were discharged, they were contacted by telephone to assess treatment adherence and an appointment was made to confirm their clinical characteristics prior to arrival in the emergency department and assess their clinical status following discharge.

Readmission to Hospital Emergency Departments in the 15 Days Following Discharge

In the subsequent review of emergency department records and interviews following discharge, the number of readmissions to hospital emergency departments occurring within 15 days of discharge was determined.

Specific Immunoglobulin E to Soy and Atmospheric Concentrations of Soy Antigen

To facilitate comparison with previous studies of patients with asthma exacerbation seen in emergency departments during the outbreaks of asthma in Barcelona, environmental concentrations of soy antigen and serum specific immunoglobulin (Ig) E were analyzed. Serum specific IgE was analyzed by radioallergosorbent test.[9] An air sampler located next to the port allowed atmospheric concentrations of soy antigens retained on a paper filter to be recorded each day. Concentrations of soy antigen were measured according to previously described methods.[10]

Episodes of Asthma Exacerbation Identified During 2002

To determine whether the incidence of asthma exacerbation seen by emergency services during the months studied was representative of the annual incidence, the same method of review of emergency service records was used to identify all episodes of asthma exacerbation seen by emergency medical services and hospital emergency departments, along with the number of patients who died as a result of asthma exacerbation during 2002.

Statistical Analysis

The frequency of asthma-related emergencies was calculated with the following formula: rate = (number of episodes × 10^5)/(number of inhabitants × number of days). The number of episodes corresponded to patients seen by emergency departments (belonging to tertiary and secondary level hospitals), emergency medical services, or the results of autopsies (taking into account that patients who died would have been seen previously by emergency services). The risk population was taken as the total population aged over 14 years who lived in the area served by the hospitals and corresponded to 1 203 598 individuals. The asthmatic population represented 6.5% of the total (78 233 individuals).

The confidence intervals (CI) for the rate were calculated assuming a normal distribution and using the following formula: CI = rate ± $Z_{a/2}$ SE, where SE = rate/$\sqrt{cases}$.

Data on the characteristics of the episodes and the patients were expressed as mean (SD) or median (interquartile range [IQR]) for continuous variables and number (%) for categorical variables. Comparisons between groups were made by *t* test or analysis of variance for normally distributed quantitative variables, Kruskal-Wallis test for quantitative variables with a nonnormal distribution, or χ^2 test for qualitative variables. Statistical analysis was performed with Stata version 7.0 (StataCorp, 2002, College Station, Texas, USA).

Results

Rate of Asthma Exacerbation Seen by Emergency Services

From the emergency departments of the 3 tertiary level hospitals we identified 1013 patient histories with diagnoses that met the established criteria. Review of the records confirmed a diagnosis of bronchial asthma in 523 episodes (51%): 276 in Hospital Universitario Vall d'Hebron, 141 in Hospital del Mar, and 106 in Hospital Clínic. In the 2 secondary level hospitals (within the area served by
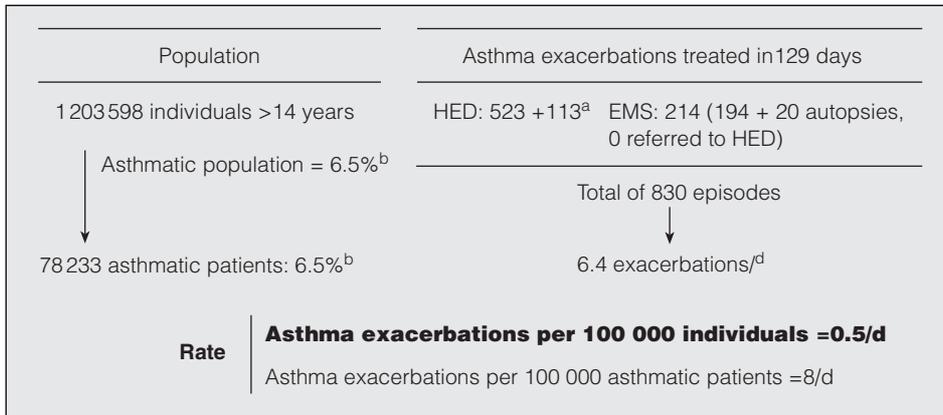
Population	Asthma exacerbations treated in 129 days
1 203 598 individuals >14 years	HED: 523 +113[a] EMS: 214 (194 + 20 autopsies, 0 referred to HED)
Asthmatic population = 6.5%[b]	
78 233 asthmatic patients: 6.5%[b]	Total of 830 episodes
	6.4 exacerbations/[d]

Rate | **Asthma exacerbations per 100 000 individuals =0.5/d**
Asthma exacerbations per 100 000 asthmatic patients =8/d

Figure 1. Rate of asthma exacerbation seen by emergency services. HED indicates hospital emergency departments; EMS, emergency medical services. [a]Secondary level hospitals. [b]Data obtained by the Spanish Group of the European Asthma Study.[15]
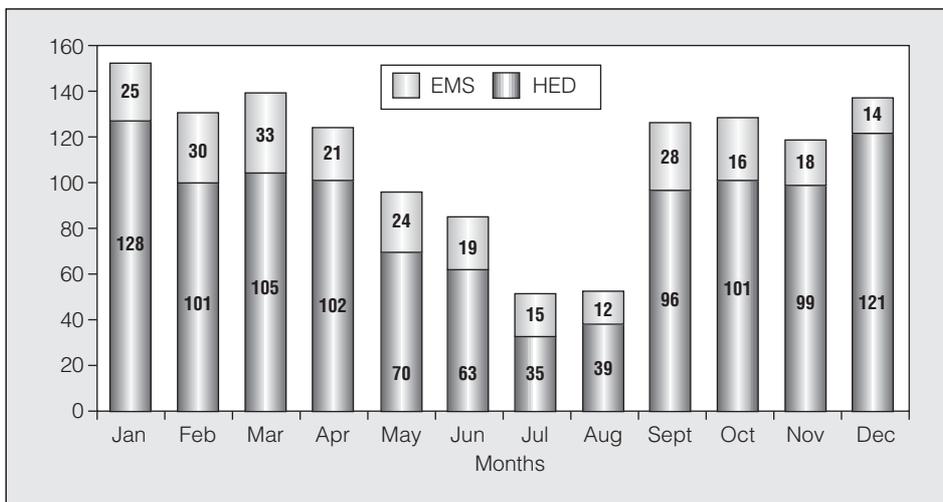

Figure 2. Rate of asthma exacerbation treated during 2002. The total number of exacerbations during the 365 days of 2002 was 2305, or 6.3 per day —4.7 per day in hospital emergency departments (HED) and 1.6 per day by emergency medical services (EMS). The daily mean from January to April was 7.9, between May and August it was 3.9, and from September to December it was 7.4.

Hospital Clínic), 113 episodes were recorded. There were 214 exacerbations identified from emergency medical service records, of which 20 (10%) were taken to hospital.

The incidence of asthma exacerbation (Figure 1) was 0.53 per 100 000 inhabitants per day (95% CI, 0.46-0.56) and 8.2 per 100 000 asthmatic patients per day (95% CI, 6.89-8.41). The incidence was 3 times higher for hospital emergency departments (0.42 per 100 000) than for out-of-hospital emergency medical services (0.12 per 100 000).

Figure 2 shows the number of exacerbations per month in 2002. The mean rate of asthma exacerbation during 2002 was 6.3 per day, very similar to the rate of 6.4 exacerbations per day recorded during the 129 days covered by the study.

Clinical Characteristics and Treatment Before and After Admission to Hospital Emergency Departments

The charts were reviewed for 276 episodes identified in the tertiary level hospitals from Monday through Thursday. In addition, following hospital discharge, an interview was carried out with 103 patients and 25 were contacted by telephone. Table 1 shows the main characteristics, notable among which is the predominance of female patients (71%), who also represented the majority of cases in which asthma exacerbation was classified as

moderate, severe, or near fatal. In contrast, male patients accounted for the majority of those in whom the exacerbation was classified as mild (*P*<.001) and in most of those cases they were young people (*P*<.001). Acute
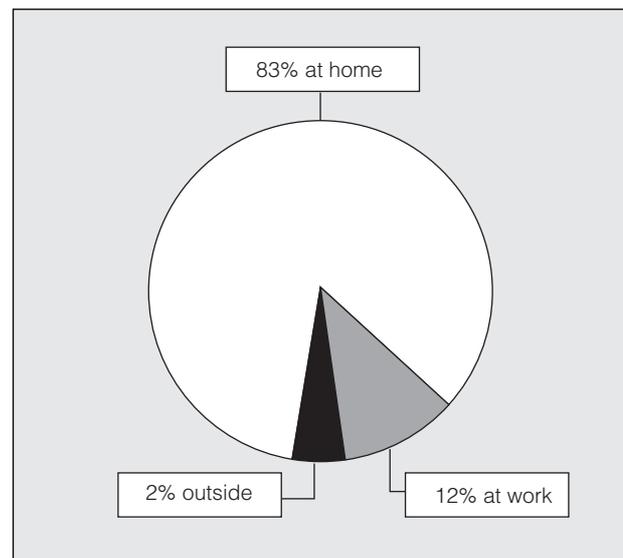

Figure 3. Location during acute onset of symptoms (n=66).

TABLE 1
Clinical Characteristics of the 276 Episodes of Asthma Exacerbation Identified in the Records of Emergency Departments of Tertiary Level Hospitals According to Sex, Age, and Severity[a]

	Total Cases (n=276)[b]	Sex			Age, y			Degree of Severity				
		Male (n=78)	Female (n=195)	P	<45 (n=119)	≥45 (n=104)	p	Mild (n=101)	Moderate (n=112)	Severe (n=43)	Near-Fatal (n=9)	P
Mean age, y	46 (20)	42 (15)	48 (21)	.026	–	–		49 (19)	54 (18)	54 (23)	39 (18)	<.001
Sex, male	78 (29%)	–	–		38 (32%)	23 (23%)	.101	39 (39%)	22 (20%)	13 (30%)	1 (11%)	.017
Smoking												
Nonsmoker	92 (40%)	19 (30%)	72 (44%)	.009	27 (27%)	50 (57%)	<.001	25 (30%)	41 (44%)	21 (62%)	2 (25%)	.009
Ex-smoker	30 (13%)	15 (23%)	15 (9%)		15 (15%)	12 (14%)		8 (10%)	15 (16%)	5 (15%)	1 (13%)	
Smoker	107 (47%)[c]	30 (47%)	75 (46%)		58 (58%)	26 (30%)		51 (61%)	38 (40%)	8 (24%)	6 (64%)	
Mean BMI, kg/m²	27.7 (7.5)	25.9 (5.0)	28.4 (8.2)	.130	25.3 (8.8)	29.9 (5.1)	.002	24.1 (4.9)	27.9 (5.3)	33.8 (12.1)	28.7 (2.8)	<.001
Charlson comorbidity index	0.08 (0.47)	0.09 (0.69)	0.07 (0.34)	.446	0.06 (0.56)	0.10 (0.36)	.032	0.02 (0.20)	0.03 (0.16)	0.26 (0.98)	0.56 (1.01)	<.001
Severity of the episode												
Mild	101 (38%)	39 (52%)	62 (33%)	.017	57 (49%)	22 (22%)	<.001	–	–	–	–	
Moderate	112 (42%)	22 (29%)	87 (47%)		45 (39%)	52 (51%)		–	–	–	–	
Severe	43 (16%)	13 (17%)	30 (16%)		12 (10%)	25 (25%)		–	–	–	–	
Near-fatal/life-threatening	9 (3%)	1 (1%)	8 (4%)		2 (2%)	3 (3%)		–	–	–	–	
Interval between onset and arrival at the hospital emergency department, h												
<1	13 (5%)	5 (6%)	8 (4%)	.728	9 (8%)	3 (3%)	.217	4 (4%)	3 (3%)	5 (12%)	1 (11%)	.010
1-4	11 (4%)	4 (5%)	7 (4%)		7 (6%)	4 (4%)		1 (1%)	7 (6%)	2 (5%)	1 (11%)	
4-8	14 (5%)	4 (5%)	10 (5%)		8 (7%)	5 (5%)		9 (9%)	2 (2%)	1 (2%)	2 (22%)	
8-24	29 (10%)	11 (14%)	18 (9%)		14 (12%)	7 (7%)		14 (14%)	12 (11%)	1 (2%)	1 (11%)	
>24	148 (54%)	39 (50%)	107 (55%)		51 (43%)	60 (58%)		46 (46%)	65 (58%)	26 (60%)	4 (44%)	
Unknown	61 (22%)	15 (19%)	45 (23%)		30 (25%)	25 (24%)		27 (27%)	23 (21%)	8 (19%)	0 (0%)	
Place of onset												
Home	55 (20%)	13 (17%)	42 (22%)	.610	31 (26%)	24 (23%)	.705	19 (19%)	26 (23%)	7 (16%)	1 (11%)	.453
Work	6 (2%)	3 (4%)	3 (2%)		4 (4%)	2 (2%)		2 (2%)	2 (2%)	2 (5%)	0 (0%)	
Street	1 (0%)	0 (0%)	1 (1%)		0 (0%)	1 (1%)		0 (0%)	1 (1%)	0 (0%)	0 (0%)	
Other	5 (2%)	1 (1%)	4 (2%)		2 (2%)	3 (3%)		0 (0%)	5 (5%)	0 (0%)	0 (0%)	
Unknown	209 (76%)	61 (78%)	145 (74%)		82 (69%)	74 (71%)		80 (79%)	78 (70%)	34 (79%)	8 (89%)	

Abbreviation: BMI, body mass index.
[a] Data are shown as mean (SD) or number of patients (%).
[b] Data not identified or not calculated due to lack of information in the emergency department records: age in 43 cases, sex in 3, smoking in 47, BMI in 178, time of arrival at hospital emergency department in 6, and severity in 11.
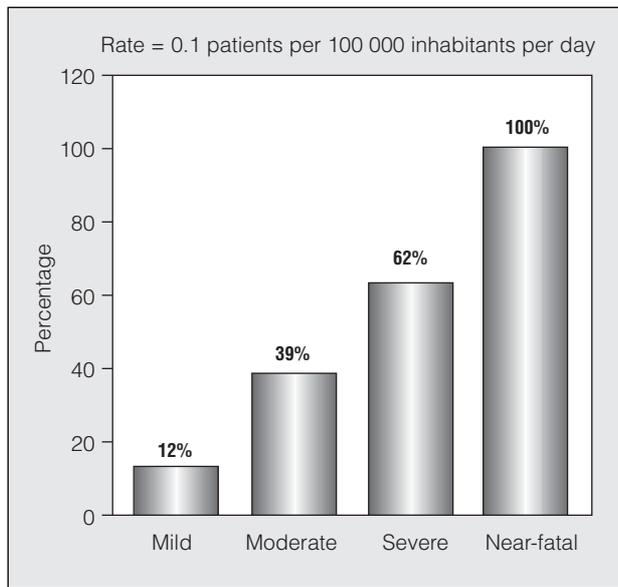[c] Seventy (31%) regular smokers and 37 (16%) occasional smokers.

Figure 4. Patients admitted to hospital (n=82, 30%) according to asthma severity.

onset of asthma exacerbation was reported by 66 patients (24%); the exacerbation began at home in 55 of those patients (83%), at work in 8 (12%), and in the street in 3 (2%) (Figure 3). Fourteen patients (5%) reported a sudden onset of the episode, which took place at home in 3 of those cases, at work in 6, and in the street in 5. In the remaining 206 patients (75%), onset was slow and it was not possible to determine when the exacerbation began. The exacerbations were considered severe in 43 patients (16%) and near fatal in 9 (3%); these patients visited the emergency department sooner than did patients with mild episodes (P=.01). The patients presented in hospital emergency departments more than 24 hours after the onset of symptoms in 54% of cases, with similar percentages at each level of severity. The Charlson comorbidity index was significantly higher (P<.001) in severe episodes (mean, 0.26 [0.98]) and near-fatal episodes (mean, 0.56 [1]). Blood pressure on arrival at the emergency departments, following exclusion of patients with known hypertension and those

with systolic blood pressure greater than 140 mm Hg or diastolic pressure greater than 90 mm Hg was 123/75 mm Hg (range, 88-140/49-90 mm Hg). Seventy patients (31%) declared themselves to be regular smokers.

The rate of hospital admission, taking into account the 636 episodes seen by emergency medical services over the 129-day study period, was 0.1 per 100 000 individuals per day. The percentages of patients who were admitted to hospital were related to severity (Figure 4). Two patients were admitted to intensive care. The Charlson comorbidity index was 0.23 (score of 23) in patients admitted to hospital and 0.08 (score of 15) in patients who were not admitted (P<.001). The comorbidity identified in admitted patients included the following: diabetes (n=6), cerebrovascular disease (n=2), peripheral vascular disease (n=2), congestive heart failure (n=2), myocardial infarction (n=1), cancer (n=1), and AIDS (n=1).

Drug treatment before and after hospital discharge is shown in Table 2. Of note was the low number of patients who received regular treatment with inhaled corticosteroids (31%) and that additional oral corticosteroids were only taken by 12% of patients in the 12 hours prior to admission.

The interviews with the patients following hospital discharge served to confirm both the diagnosis and the treatment following discharge, as well as to identify recurrences (Table 2).

Readmission to Hospital Emergency Departments in the 15 Days Following Discharge

The 276 episodes included 28 recurrences (10%) in 23 patients (1 patient with a BMI of 64 kg/m² had 3 recurrences and another patient had 2). Therefore, the total number of patients treated was 253. The patients in whom recurrences were recorded had the following characteristics: age, 63 years (range, 22-89 years); 19 (72%) women; BMI, 29 kg/m² (range, 15-64 kg/m²); and Charlson index of 0.07 (score of 2; only 2 patients had a history of myocardial infarction). Four of the episodes were classified as mild, 14 moderate, 6 severe, and 4 near fatal. Table 2 shows the treatment received at discharge both by patients with recurrences and by those without. The only significant difference was a lower rate

TABLE 2
Drug Treatment Prior to Admission (n=276) and Following Discharge (n=181)

Drug Treatment	Prior to Admission		Following Discharge	
	Chronic	Administered in the Last 12 h	No Recurrences (n=153)	Recurrences (n=28)
Inhaled β₂-agonists	232 (84%)	164 (59%)	130 (84%)	28 (100%)
Inhaled corticosteroids	85 (31%)	0	123 (80%)	28 (100%)
Ipratropium bromide	30 (11%)	5 (2%)	80 (52%)	1 (4%)ᵃ
Antileukotrienes	19 (7%)	4 (1%)	11 (7%)	3 (11%)
Antihistamines	13 (5%)	0	3 (2%)	0
Theophylline	17 (6%)	0	14 (9%)	2 (7%)
Oral corticosteroids	10 (4%)	33 (12%)	88 (57%)	14 (50%)
Intravenous corticosteroids	0	0	0	0
Antibiotics	0	0	52 (34%)	2 (7%)ᵇ
Subcutaneous or intravenous β₂-agonists	0	0	0	0
No treatment	23 (8%)	0	0	0

ᵃ P<.0001 ᵇ P<.001

of prescription of ipratropium bromide and antibiotics in those with subsequent recurrence ($P<.0001$ and $P<.001$, respectively). The mean blood pressure in 85 of the 103 patients interviewed following discharge, once those with systolic pressures above 140 mm Hg or diastolic pressures above 90 mm Hg had been excluded, was 112/71 mm Hg (range, 90-130/64-95 mm Hg).

Serum Specific Immunoglobulin E Concentrations and Atmospheric Levels of Soy Antigen

Only 9 patients (8%) had IgE concentrations above the cutoff. The mean atmospheric concentration of soy antigen was 37 U/m³, and peaks of more than 160 U/m³ were not recorded on any day.

Episodes of Asthma Exacerbation Identified During 2002

As shown in Figure 2, the mean frequency of asthma exacerbations per day in 2002 was 6.3, a similar rate to the 6.4 episodes per day observed over the 129 days of this study.

Discussion

The number of asthma exacerbations requiring medical attention in this study was 0.5 episodes per 100 000 individuals per day. This is the first study to assess the number of asthmatic patients treated in hospital emergency departments and by out-of-hospital emergency medical services in a specific city. The mean of 6.4 asthma exacerbations per day during the 129 days of the study is representative, on the basis that it is very similar to the mean of 6.3 episodes per day recorded over the whole year. This information could be used in future studies as a reference for analysis of the degree of control of the disease in asthmatic patients and the quality of health care provided in Barcelona, since improved clinical management will lead to a reduction in the number of asthma exacerbations[22] and therefore in the need for hospital care.[23] In 1998-1999, the mean number of asthma exacerbations seen each day only in hospital emergency departments was 4.2 (in a population of 1 245 060 individuals).[10] Given that in Europe the number of asthmatic patients has doubled in the last 10 years[1] and that the atmospheric levels of soy antigen in Barcelona are currently the same as in 1989, when there were no asthma outbreaks (in other words, the levels are very low), asthma is clearly better controlled in the asthmatic population of Barcelona now than it was in 1989. In addition, information on the rate of asthma exacerbation may lead to suspicion of trigger factors such as, for instance, soy antigen, fungal spores, or other agents that could lead to episodes of asthma.

Around 20% of all asthma exacerbations were seen by emergency medical services. The present analysis has allowed a more accurate estimate of the true rate of asthma exacerbation. In addition, given that a large percentage of deaths due to asthma occur outside hospital emergency departments,[24] to establish mortality it was necessary to use not only information regarding out-of-hospital emergency medical services but also to review the autopsies performed in the city.

Only 31% of patients were taking inhaled corticosteroids, a percentage that is lower than the 50% observed by our group in patients managed in primary care in our area.[25] Inhaled corticosteroids are well known to be highly effective for controlling asthma and reducing the rate of both asthma exacerbation[26] and asthma-related hospital admission,[23] and specifically, that they are effective in preventing episodes of life-threatening asthma[27] and related deaths.[28] In addition, the investigating physician only recorded use of inhaled corticosteroids if it was included in the patient's chart or reported by the patient; this probably prevents conclusions regarding whether the patients actually took the drug on a regular basis. If we add to this the frequency of incorrect inhaler technique, which has been reported to occur in 19% and 30% of cases in a study of Spanish patients using 2 different inhaler devices,[29] the extent of inadequate treatment in patients with symptoms of asthma exacerbation can be considered alarming. This low frequency of use of inhaled corticosteroids is well described in the literature and represents one of the main causes of exacerbation.[22,26] Inappropriate preventive treatment and poor treatment adherence have also been reported in, respectively, 31% and 21% of children seen in a hospital.[30] This situation also leads to enormous health expenditure, particularly when patients must ultimately be admitted to hospital.[31]

Likewise, only 30% of patients who suffered near-fatal episodes of asthma were taking inhaled corticosteroids; this percentage is lower than the 57% observed in a multicenter study in Spain that used the same definition of a near-fatal episode.[17] A study undertaken in France found that 47% of such patients received inhaled corticosteroids, although the criteria used to define near-fatal episodes were less restrictive.[18]

Although early use of oral corticosteroids reduces the number of hospital admissions,[32] only 12% of patients had taken them in the 12 hours prior to admission in emergency departments, despite 54% of asthma exacerbations having begun 24 hours prior to visiting the emergency department (Table 1). Only 29% of patients who suffered near-fatal episodes had received oral corticosteroids. This percentage was even lower in a study performed in Spain by Plaza et al.[17]

In our study, we observed a higher proportion of women suffering asthma exacerbations (71%), as has also been observed in other studies.[33,34] It was also found that there was a highly significant predominance of female patients (8:1) suffering episodes of near-fatal asthma, a finding which differs from the results of a study of patients with near-fatal asthma in Spain[17] and from the results of other studies,[18] where the percentage of women was found only to be slightly higher than that of men.

It is also worth noting the high percentage of patients who were regular smokers (31%), a rate that is comparable to the results of Salmeron et al[18] in France. In the same year, the percentage of smokers among asthmatic patients seen in primary care centers in our area was 17%.[25] It should be noted that the proportion of smokers among those who suffered severe episodes (24%) was lower than

among those patients in whom exacerbation was classified as moderate (40%) or mild (61%). Therefore, even taking into account that the patients with mild episodes were younger and that among them there were more smokers, it appears that smoking did not play a significant role in triggering severe asthma exacerbations. In contrast, in the patients with near-fatal episodes, the percentage of smokers was higher (64%) than in those of a similar age with severe episodes.

In terms of the severity of the episodes, 37% were classified as mild, 41% moderate, 16% severe, and 3% near fatal. These percentages differ from the results of Salmeron et al[18] (26% of episodes were mild or moderate, 49% severe, and 26% near fatal) even though the criteria for classification were similar but not identical to those described in that study (eg, the French study did not take into account blood gas values). These differences may be due, among other factors, to differences between the primary care systems in the 2 countries. It is possible that in the French system mild or moderate exacerbations are more often treated in primary health care centers. It is also quite likely that our use of the GINA classification was more restrictive in the categorization of episodes of severe exacerbation. In a review of the few studies that have been done, McFadden,[36] after stating that the incidence and prevalence of severe episodes are unknown, reported a rate of 21% for severe episodes and 5.1% for near-fatal episodes, percentages that are similar to those obtained in our study.

Regarding BMI, the patients with mild exacerbation who were seen in hospital emergency departments were significantly younger and therefore generally had a normal BMI. With increasing severity of the episode, the patients were generally older and had a significantly higher BMI. The highest BMI was seen in patients with severe exacerbation (P<.0001), as described in other studies.[37,38] The rate of hospital admission (30% of patients seen by emergency services) was 0.1 per 100 000 individuals per day, lower than the 0.8 per 100 000 estimated in hospitals in Chicago[19] and also different to the rate in French hospitals, where 54% of patients were admitted.[18] It should be remembered that in our study patients were considered to have been admitted if they remained in hospital for more than 24 hours, partly explaining the rate of 12% in patients with mild asthma exacerbation. As expected, 100% of the patients who were seen by emergency services with a life-threatening asthma attack and more than half those with severe episodes were admitted, findings that support the criteria used for classification of the severity of asthma exacerbations.

The Charlson comorbidity index[21] was significantly higher in patients with severe or near-fatal episodes, a situation that would almost certainly have favored hospital admission. Therefore, in studies of hospital admission for asthma exacerbations, associated diseases in asthmatic patients should also be taken into account, a factor that has not been reported previously.

The rate of readmission to hospital emergency departments in the 15 days following discharge was lower at 10% than that mentioned in other studies (12%-16%).[40] The treatment with inhaled and oral corticosteroids prescribed for these patients when they were discharged was similar to that given to other patients, as also observed by Emerman et al,[41] although they were less often prescribed ipratropium bromide and antibiotics (Table 2), an observation that in the case of ipratropium bromide we have not found reported elsewhere in the literature. Regarding the use of antibiotics, the TELICAST trial[42] recently showed beneficial effects of telithromycin in asthma exacerbations.

The results of our study also confirm the effectiveness of the preventive measures adopted during the unloading of soybeans, since the serum concentrations of specific antibodies were found to be elevated in only 8% of patients, a slightly higher percentage than the 4.6% found in the cases of asthma exacerbation seen in emergency departments on a day without an outbreak in the 1980s.[9] Furthermore, the mean atmospheric concentration of soy antigen was very low at 37 U/m^3, and peaks of more than 160 U/m^3 were not recorded on any day.

In conclusion, we have provided the first estimates of the rate of asthma exacerbation. It was found that in around a quarter of cases onset was acute and in 5% it was sudden, and that 16% of episodes were severe and 3% life threatening. Furthermore, an alarming rate of inadequate treatment was observed. We also found that patients with severe asthma were more obese and that the rate of hospital admission was directly related to the severity of the exacerbation. The presence of comorbidity influenced hospital admission. The atmospheric levels of soy were low, thus confirming the effectiveness of preventive measures adopted during the unloading of soybeans. Further studies should be performed to determine the usefulness of repeated measures of the rate of asthma exacerbation as an indicator of the level of control of asthma in a given population.

Acknowledgments

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