

Undertreatment in a nonselected population of adult patients with asthma

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Background and aim: The question of undertreatment has frequently been raised concerning the management of asthma but, to date, very few studies have been carried out. In those studies that have been performed, the methodology was inadequate because they were conducted on a selected population of patients with asthma or by interviewing doctors. As part of the European Community Respiratory Health Survey, nonselected patients with asthma (22 to 44 years old) in two French cities (Paris and Montpellier), were examined to assess possible undertreatment.

Methods: Patients with asthma were recruited according to a positive response to questions on asthma in a questionnaire and a positive methacholine challenge. The severity of asthma was assessed by a cumulative score, which has previously been shown to be significantly correlated with the validated clinical score of Åas. Patients were asked to attend the clinic and bring with them any medications that they regularly received. The optimal treatment of asthma was based on the International Consensus Report on the Management of Asthma.

Results: According to the international guidelines, among the patients who required antiinflammatory treatment, 86.4% were undertreated in Paris and 66.7% were undertreated in Montpellier ($p < 0.03$, chi square test). Moreover, among the patients with severe asthma, 85% and 60%, respectively, were not receiving an antiinflammatory treatment.

Conclusion: This study is the first to highlight the magnitude of undertreatment of patients with asthma in a nonselected population. (*J Allergy Clin Immunol* 1996;98:514-21.)

Key words: Asthma, epidemiology, undertreatment

Most statistics relating to asthma show that there has been an increase in the prevalence and morbidity and mortality rates over the past 20 years.¹⁻⁶ The reasons for the increased morbidity

Abbreviation used

ECRHS: European Community Respiratory Health Survey

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These results come from a local analysis of data collected for the European Community Respiratory Health Survey. Any final international comparison may use a different form of analysis. The study will be subject to further checking by the Coordinating Centre for the study.

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and mortality rates are not completely understood but may be attributed to several factors including underrecognition of asthma, poor recognition of the severity of asthma by patients and doctors, and undertreatment.^{2-4, 7-9} These trends have led to the publication of several Consensus Reports on the Management of Asthma.^{7, 10-14} Although airway inflammation is still incompletely understood in asthma and some criticisms on the effects of corticosteroids remain,¹⁵ these consensus reports are based on studies showing that antiinflammatory drugs in general, and inhaled corticosteroids in particular, improve the control of asthma in adults and children.¹⁶⁻²⁰ These recommendations stress the importance of prescribing treatment with anti-

inflammatory drugs early in the disease and continuing their use for a prolonged period.

Undertreatment of patients with asthma is commonly observed throughout the world and consistently proposed as a key pejorative factor; however, only a few studies have been performed, mostly in children, and they are insufficient for assessment of the magnitude of the problem.^{8, 21-24} In particular, some studies have examined the treatments prescribed by doctors for their patients with asthma but not the treatments the patients were actually taking. Because compliance with the use of inhalers is a major problem in asthma,²⁵ studies based on doctors' reports are likely to overestimate the actual treatment received by patients with asthma.

The categorization of the severity of asthma is a difficult problem that remains to be completely resolved. Several methods have been used, but very few scores have been validated. Pulmonary function can be used to determine the current severity of the disease, but a single measure does not take into account long-term severity. Nonspecific bronchial hyperreactivity assessed by nonspecific challenges and/or the variability of the peak flow provide better estimates.²⁶⁻³⁰ The long-term severity of asthma is, however, based on scores that combine symptoms, treatments, peak flow rates, and/or pulmonary function.^{10, 13, 14, 31-34} Although there is no optimal score, the Åas score has been validated because it has previously been shown to be correlated with FEV₁,³⁵ eosinophilic inflammation,^{35, 36} other markers of inflammation,³⁷⁻³⁹ and quality of life.⁴⁰

A population study (European Community Respiratory Health Survey [ECRHS]) has been implemented to assess the prevalence and risk factors of asthma and asthma-like symptoms in several areas in different countries by using a standardized protocol. This study consisted of two stages: a postal questionnaire sent to representative samples of populations (stage 1) and a full-length questionnaire with examination of subsamples of the subjects who answered the postal questionnaires.^{41, 42}

A study was carried out in two French cities (Montpellier and the eighteenth district of Paris), which participated in the ECRHS, to assess the treatment of a population of nonselected patients with asthma. Asthmatic patients were identified by means of a postal questionnaire sent to a representative sample of the population in each city. Subjects were asked to come to the clinic for evaluation of asthma with the drugs they were

currently taking. The severity of asthma was measured in Montpellier by using the Åas score,³¹ which is used to validate a calculated severity score. The optimal treatment of asthma was defined according to the severity of asthma measured by the calculated severity score and taking into account the recent recommendations of the International Consensus on the Diagnosis and Treatment of Asthma.¹⁴ This was then measured against the actual treatment the patients were receiving to characterize any possible under- or overtreatment.

METHODS

The instruments

The methods used have been previously described in detail.⁴² Briefly, the postal questionnaire (stage 1) included nine questions on asthma attacks, medication taken over the last 12 months, and asthma-like symptoms. The full-length questionnaire used in stage 2 included more detailed questions on asthma and bronchial symptoms, based on bronchial questions used by the International Union Against Tuberculosis and Lung Diseases questionnaire.⁴³⁻⁴⁵ Assessment of smoking habits was adapted from the American Thoracic Society questionnaire.⁴⁶ The questions were validated in the United Kingdom and other European countries.⁴⁵ Questions on medication taken for asthma over the last 12 months were devised especially for the ECRHS study. Lung function tests and bronchial challenge were performed with a computerized spirometer (Biomedin Srl, Padova, Italy). Methacholine challenge was carried out with a Mefar MB3 dosimeter (Mefar Srl, Bovezzi, Italy). The challenge was continued until a cumulative dose of 4 mg had been given or until a PD₂₀ was reached.

Population

The two study centers were the whole city of Montpellier and the eighteenth district of Paris, France. The areas were selected according to the guidelines of ECRHS, that is, by using preexisting administrative boundaries with total population of around 150,000 from which a representative sample of a minimum of 3000 subjects (1500 of each sex), aged 20 to 44 years, should be included in the study. Electoral rolls were used as a sampling frame. Because electoral rolls are not constantly updated, subjects who were not found at their registered address were considered as outside the sampling frame and not eligible to participate in the study. Random samples were obtained by simple random sampling in Paris and stratified by sex in Montpellier.

Stage 1

Three thousand seven hundred seventy-four subjects in Montpellier and 3152 subjects in Paris responded to the postal questionnaire (response rates: 69% and 74%, respectively). Among them, 182 respondents in Montpellier (4.8%) and 156 in Paris (4.9%) gave a positive

TABLE I. Scoring system of asthma severity

FEV ₁ (% predicted)	No. of asthma attacks in last 12 months			
	≤5	6-10	11-30	>30
≥90	1	2	2	3
80-89	2	2	3	4
70-79	3	3	4	4
<70	4	4	4	4

The first score is calculated by the number of asthma attacks in the last 12 months, and FEV₁ is measured as percentage of predicted value. To obtain the final score, add 1 if patient is receiving antiinflammatory treatment (first step); add 1 to score 1 if patient has wheezing and shortness of breath at rest; add 1 to score 2 if the two above symptoms are present, plus waking up with tightness in the chest, and being woken by an attack of shortness of breath (second step).

answer to at least one of these two questions: "Have you had an attack of asthma in the last 12 months?" and "Are you currently taking any medicine (including inhalers, aerosols, or tablets) for asthma?" These subjects were designated as "patients with asthma".

Stage 2

Stage 2 was part of the standard protocol. All subjects who replied to the postal questionnaire were asked to come to the University clinic. Four hundred fifty-six subjects in Montpellier and 660 subjects in Paris participated in stage 2. Among the participants, 48 (10.5%) were diagnosed as having asthma in Montpellier and 46 (6.9%) in Paris. The comparison between participants with asthma and nonparticipants did not show any difference in regard to mean age, gender, proportion of subjects currently taking medicine for asthma, or proportion of positive responses to any of the following questions referring to the last 12 months: wheezing, being woken by an attack of shortness of breath, or coughing.

In addition to these identified patients with asthma, we considered as nondiagnosed patients with asthma those subjects who had a positive response to methacholine challenge ($PD_{20} \leq 4$ mg), had smoked less than 12 pack/years, and had given a positive answer to at least one of the following questions from the full-length questionnaire:

- Have you had wheezing or whistling in your chest at any time in the last 12 months?
- Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 months?
- Have you been woken by an attack of shortness of breath at any time in the last 12 months?

Twenty-six subjects in Montpellier and 20 subjects in Paris were assigned to the this category of "nonidentified patients with asthma."

Assessment of severity of asthma

The severity of asthma was assessed in Montpellier by the Åas score³¹ and in both cities according to the full-length questionnaire completed during the examination together with the results of the pulmonary function tests (FEV₁ and PD₂₀). The scoring of asthma severity was not part of the standard protocol.

The score of Åas³¹ grades the different forms of chronic asthma on the basis of the events that took place during the previous year and combines symptoms (number and duration of asthmatic episodes, total duration of symptoms, presence or absence of symptom-free intervals between attacks) and the requirements for medication. The score ranges from very mild (score 1) to very severe (score 5) forms of asthma but does not take into account the pulmonary function of the patients.

A calculated scoring system was used in both cities and was done with the Åas score. This system is described in Table I. A first score, ranging from 1 to 4, was calculated from the number of asthma attacks in the last 12 months, and FEV₁ was measured as a percentage of predicted values. Then, we added 1 if the patient had received antiinflammatory treatment because this has been shown to improve symptoms and FEV₁ (first step of final score). Finally, we took asthma-like symptoms into account when the first score was 1 or 2, as explained in Table I. This score was validated in Montpellier compared with the Åas score. There was a highly significant correlation between the severity of asthma assessed by the score of Åas and by the calculated symptom-medication score derived from the questionnaire for the patients with asthma in Montpellier ($n = 74$; $\rho = 0.61$, $p < 0.0001$, Spearman's rank correlation).

In the analysis, owing to a relatively low number of patients with severe asthma, patients were assigned to three categories: mild (calculated score of 1), moderate (calculated score of 2), and severe (calculated scores of 3 and over).

Assessment of optimal treatment

Patients were asked to "come with the drugs taken the day before the visit" because many patients cannot remember the names of their drugs. Moreover, in the questionnaire we asked whether they were taking the drugs regularly or on demand, the dose used, and the duration of the treatment. We also enquired whether other drugs were taken. We were unable to obtain the prescriptions because of the French system of compensation for medical costs.

Depending on the severity of asthma, as defined by the score presented previously, it was possible to identify the optimal treatment suggested by the recommendations of the International Consensus on the Diagnosis and Management of Asthma.¹⁴ Patients with mild asthma should not receive any antiinflammatory treatment. Patients with moderate asthma should receive long-term antiinflammatory treatment with disodium cromoglycate, nedocromil sodium, or low-dose inhaled

TABLE II. Characteristics of patients

	Montpellier		Paris	
	Diagnosed (n = 48)	Nondiagnosed (n = 26)	Diagnosed (n = 46)	Nondiagnosed (n = 20)
Age (yr)*	32.6 ± 8.2	32.2 ± 6.4	33.6 ± 7.7	33.4 ± 7.9
Sex (% male)	46.2	41.7	43.5	15.0
Severity of asthma				
Mild (%)	31.2	65.4	32.6	70.0
Moderate (%)	37.5	30.8	30.4	20.0
Severe (%)	31.2	3.8	37.0	10.0
FEV ₁ (% predicted)*				
Mild	108.3 ± 8.1	104.3 ± 7.8	106.3 ± 9.1	103.6 ± 7.1
Moderate	107.2 ± 11.2	98.5 ± 11.6	100.0 ± 11.4	98.3 ± 12.4†
Severe	85.2 ± 13.5	86.0†	76.2 ± 11.0	80.0 ± 5.7†
PD ₂₀ (μg)*				
Mild	351.6 ± 618.7	1539.8 ± 1321.9	634.9 ± 869.5	920.2 ± 1275.4
Moderate	819.9 ± 1286.3	812.7 ± 552.4	261.1 ± 499.0	632.6 ± 877.8†
Severe	404.9 ± 480.5	20.0†	232.4 ± 462.8	978.4 ± 1261.3†

*Mean ± SD.

†Numbers less than 5.

corticosteroids (up to 400 μg of equivalent dose of beclomethasone). Patients with severe asthma (calculated scores of 3 and 4) should receive long-term treatment with high doses of inhaled corticosteroids. Undertreatment was graded. Patients with moderate asthma not receiving antiinflammatory treatment as defined by the International Consensus or patients with severe asthma receiving low-dose inhaled corticosteroids were graded as "undertreatment, step 1." Patients with severe receiving no antiinflammatory treatment were graded as "undertreatment, step 2." On the other hand, patients receiving a more intensive antiinflammatory treatment than proposed by the guidelines were graded as "overtreatment."

RESULTS

Characteristics of the patients

The characteristics of the patients are shown in Table II. Patients who were diagnosed and nondiagnosed by postal questionnaire were separated. The proportion of nondiagnosed patients was similar in both cities (35% and 30%). The distribution according to the severity of asthma was also similar in both cities, as was the education level of the patients studied.

Treatment of the patients

No patient was found to be overtreated. On the other hand, 62% of patients who required antiinflammatory treatment according to the international guidelines were undertreated in Montpellier and 86% of patients in Paris ($p < 0.02$, chi square test). Moreover, among the patients with severe

asthma, 62% and 84%, respectively, were not receiving any antiinflammatory treatment (Fig. 1). The proportion of patients who used β_2 -agonists was greater in undertreated patients than in those who were not undertreated in both cities: 73% versus 46% in Montpellier ($p = 0.05$) and 66% versus 41% in Paris ($p = 0.05$).

DISCUSSION

This study shows for the first time in a nonselected population of patients with asthma that most patients who should receive antiinflammatory treatment according to international guidelines are undertreated.

The major interest of this study is that the population was not selected according to health care attendance. Data collection for such a study needs valid and standardized instruments. The European Community epidemiology questionnaire has been derived from the International Union Against Tuberculosis and Lung Diseases questionnaire^{43, 44} and the Epidemiology Standardization Project of the American Thoracic Society⁴⁶ and has been thoroughly discussed at several committee meetings. Although there is no perfect questionnaire applicable to asthma, the ECRHS questionnaire appears to be the most widely accepted. In France, the selection of subjects on the basis of electoral lists appears to be an acceptable sampling frame. We used the same selection methods in both cities. Patients with asthma were selected on

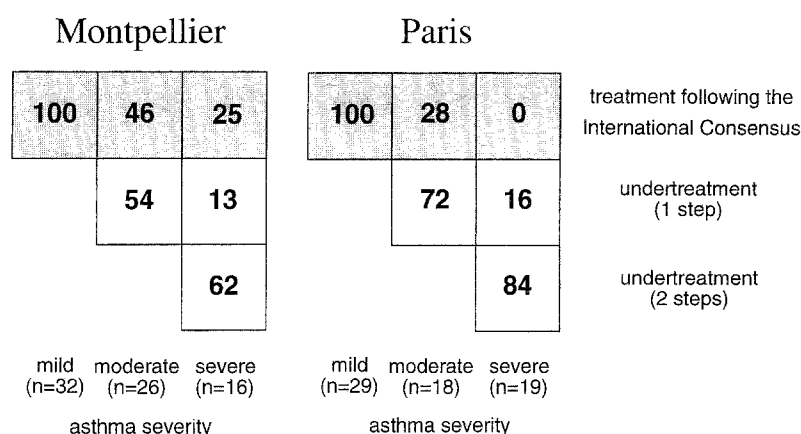


FIG. 1. Global results expressed in percentage.

the basis of responses to the most relevant questions pertinent to asthma in the full-length questionnaire and a reversible airway disease assessed by a standardized methacholine challenge. Subjects fulfilling these criteria who had smoked over 12 pack-years were excluded because it is unlikely that chronic bronchitis would have developed in subjects who had smoked less.^{47, 48}

The rate of response to the postal questionnaire was similar in both cities and was satisfactory for a postal survey in a general population sample. As expected for an examination that lasts over 2 hours in hospital, the participation rate in stage 2 was much lower than that in stage 1 and was greater among patients with asthma than nonasthmatic subjects. However, there was no self-selection of either the most severe or the most undertreated patients with asthma because the comparison of participant and nonparticipant subjects with asthma showed that those who attended the examination were no different from those who did not attend, especially in regard to the frequency of asthma-like symptoms in the last 12 months or current medications for asthma. The percentage of patients with severe asthma was 21.6% in Montpellier and 28.8% in Paris. Because there are no definite data concerning the general population, we do not know whether there was a selection bias. In both cities there were fewer patients with severe asthma than patients with mild asthma.

Taken together, these criteria indicate that the study is valid and that we studied a nonselected population of patients with asthma. However, only a fraction of persons with possible asthma were examined, and the sampling frame may not therefore be completely representative of the French population of patients with asthma.

The study was designed to compare the actual and optimal treatments of asthma before guidelines on the management of asthma had been published in French. It was therefore necessary to assess the severity of asthma. We were unable to use the proposals of the International Consensus on Asthma because the study started before the report was published. For many years, we have attempted to categorize patients with asthma. First, we used pulmonary function, but it was rapidly found that this was insufficient. We and others have used the Åas score, which although not perfect, seems to be the most suitable for categorizing patients. The score of Åas was used in Montpellier and not in Paris because patients were seen in a clinic in Montpellier and in an epidemiologic center in Paris, and it was believed that only physicians could use the Åas score. However, we found a significant correlation between the score of Åas and the calculated score we propose. Thus it seems that the categorization of patients was as good as possible. In Montpellier the Åas score³¹ was compared with responses to relevant questions of the full-length questionnaire and the results of FEV₁. We observed a highly significant correlation between the Åas score and the calculated score. We then used the same calculation for both cities. We could have used bronchial hyperresponsiveness as an independent indicator of severity. PD₂₀ has been used to assess the severity of asthma by some authors. A significant correlation between the severity of asthma and bronchial hyperresponsiveness has been observed,^{49, 50} but there are some concerns because the overall correlation in a group of subjects may not necessarily apply to individual patients.⁵¹⁻⁵³ These correlations have been mainly shown in children, and patients with a low FEV₁

may have a falsely increased bronchial hyperreactivity. There are some studies showing that severity of bronchial hyperreactivity tends to increase with asthma severity, but there are many patients who do not follow these trends. Some authors have correlated PD₂₀ with medication requirements.⁵⁴⁻⁵⁷

The assessment of optimal treatment of patients with asthma presents another problem. Several consensus reports have agreed that antiinflammatory treatment represents the cornerstone of the management of chronic asthma.^{7, 10-14} Although the proposals of these guidelines have not been fully validated, inhaled corticosteroids are recommended because their use is associated with a reduction in the number of hospitalizations⁵⁸ and an improvement in the control of asthma in adults and children.¹⁶⁻²⁰ We selected the International Consensus on the Management of Asthma¹⁴ because it is the most recent guideline for adult patients with asthma and is widely accepted. Although we did not use the categorization of the severity of asthma outlined in the International Consensus Report, it seemed appropriate to use these guidelines because the cutoffs for FEV₁ are similar in our scoring system and in the International Consensus Report and because our patients have been classified into categories that overall correspond to those of the International Consensus Report.

Undertreatment of patients with asthma was recognized many years ago; however, most studies have been carried out in children, and none of them used the criteria set by the International Consensus of Asthma.¹⁴ Kaptein et al.²² found that most children, even if they had severe asthma, did not receive any treatment, and school absenteeism fell 10-fold in the 31 children offered continuous prophylactic treatment. Hill et al.⁸ found that patients with severe asthma were usually undertreated because 70% of the children who were absent from school for more than 10 days were not taking any drugs or were taking only β -agonists. Bauman et al.²³ in a large population sample of primary school children and adults, found that undertreatment was relatively common. These authors⁵⁹ compared undertreatment from their survey and found that optimal asthma management was apparently more common in the general practitioners' attendees. However, it was observed that the better management by general practitioners was due to a bias in physicians' selection of patients. Neville et al.²⁴ found that bronchodilators were more commonly used than antiinflammatory treatments in children. Thus although undertreat-

ment was expected, few data were available for adults. In Paris and Montpellier, respectively, 86% and 62% of patients with asthma who should receive antiinflammatory treatment were being undertreated. Moreover, 84% and 62% of patients with severe asthma were not receiving any antiinflammatory treatment in Montpellier and Paris, respectively. These patients are at high risk for acute exacerbations.^{1-4, 7, 8} Differences were observed between Paris and Montpellier, but they cannot be explained by a difference in school education, demographics, or access to medical services, which are similar in both cities. Thus studies of undertreatment carried out from doctors' questionnaires or prescriptions are underestimating the problem as suspected.

This study highlights the importance of guidelines for the treatment of patients with asthma, which should be more widely disseminated in an attempt to increase the administration of antiinflammatory drugs that are likely to reduce the morbidity and mortality rates of asthma¹⁻⁴ and the accelerated decline in pulmonary function.^{19, 60} This study shows the importance of using guidelines and specific measures in the diagnosis of asthma to avoid undertreatment.

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