Factors Associated With Severe Uncontrolled Asthma and the Perception of Control by Physicians and Patients

María del Carmen Vennera, a,b,c,∗ César Picado, a,b,c Lys Herráez, d Jordi Galera, d Jordi Casafont, d on behalf of the Study Group CONTROL

Article history:
Received 19 November 2013
Accepted 13 March 2014
Available online 16 July 2014

Keywords:
Asthma
Control
Risk factors
Patients
Spanish Guidelines for Asthma Management

Abstract
Introduction: Despite current treatments, more than half of patients with asthma are not controlled. The objective was to evaluate the correlation between control perceived by patients and physicians, compared with control evaluated according to criteria of the Spanish Guidelines for Asthma Management (GEMA), and to investigate the factors associated with that control.

Methods: Multicenter, cross-sectional, observational study including 343 patients with severe persistent asthma according to GEMA criteria seen in the Department of Pulmonology and Allergology. The correlation between asthma control perceived by the patient, the physician and according to clinical judgment based on the GEMA criteria was calculated, and a multivariate analysis was used to determine variables related to the perception of asthma control.

Results: According to GEMA criteria, only 10.2% of patients were well controlled, 27.7% had partial control and 62.1% were poorly controlled. Both the physicians and the patients overestimated control: 75.8% and 59.3% of patients had controlled asthma according to the patient and the physician, respectively, and were not controlled according to GEMA (P<.001). Patients with uncontrolled asthma according to GEMA had higher body mass index (P=.006) and physical inactivity (P=.016). Factors associated with a perceived lack of control by both physicians and patients were: nocturnal awakenings (≥1 day/week), frequent use of rescue medication (≥5 days/week) and significant limitation in activities. Discrepant factors between physicians and patients were dyspnea and emergency room visits (patients only), FEV1≤80% and a poorer understanding of the disease by the patient (physicians only).

Conclusions: Only 10% of patients with severe asthma evaluated in this study are controlled according to GEMA criteria. Patients and physicians overestimate control and the overestimation by patients is greater. Physical inactivity and obesity are associated with a lack of control according to GEMA.

© 2014 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.

Factors asociados con el asma grave no controlada y con la percepción del control por parte de médicos y pacientes

Introducción: A pesar de los tratamientos actuales más de la mitad de pacientes con asma no están controlados. El objetivo fue evaluar la concordancia entre la percepción de control por parte de pacientes y médicos comparado con el control evaluado según criterios de la Guía española para el manejo del asma (GEMA), así como investigar los factores asociados con dicho control.

Métodos: Estudio multicéntrico, observacional y transversal que incluyó 343 pacientes con asma grave persistente según criterios de la GEMA atendidos en consultas de neumología y alergología. Se calculó la concordancia entre control del asma según percepción del paciente, criterio clínico del médico y en

Palabras clave:
Asma
Control
Factores de riesgo
Pacientes
Guía española para el manejo del asma

∗ Please cite this article as: Vennera M C, Picado C, Herráez L, Galera J, Casafont J, en nombre del Grupo de Estudio CONTROL. Factores asociados con el asma grave no controlada y con la percepción del control por parte de médicos y pacientes. Arch Bronconeumol. 2014;50:384–391.

E-mail address: cvennera@clinic.ub.es (M.C. Vennera).

http://dx.doi.org/10.1016/j.arbr.2014.06.017
1579-2129/© 2014 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.
function of criteria GEMA, and it utilized analysis multivariate to determine variables related with the perception of control of the asthmatics. Results: According criteria GEMA the 10.2% of patients were well controlled, the 27.7% presented control parcial and the 62.1% was mal controlled. Tanto médicos como pacientes sobrestimaron el control: el 75.8 y 59.3% of individuos with asma controlada según el propio paciente y su médico, respectivamente, no estaba controlada según GEMA (p < 0,0001). Los pacientes con asma no controlada según GEMA presentaron a mayor índice de masa corporal (p = 0,006) and más sedentarismo (p = 0,016). The factors associated to the lack of control perceived both by physicians and by patients were: despertares nocturnos ($\geq$ 1 día/semana), use frecuente of medicación de rescate (p =0 días/semana) and limitation importante of activities. The factors discordantes among médicos and pacientes were: disnea and visitas a urgencias (solo pacientes); FEVI $\leq$ 80% and poor knowledge of the enfermedad by el paciente (solo médicos). Conclusions: The 10% of patients with asma grave evaluated in this study está controlado according criteria GEMA. Tanto pacientes como médicos sobrestiman el control, with a major overestimation in patients. El sedentarismo and the obesity se asocian con la falta de control según GEMA. © 2014 SEPAR. Published by Elsevier España, S.L.U. Todos los derechos reservados.

Introduction

The prevalence of asthma in Spain is approximately 5%.1 Most patients have mild or moderate disease that can be controlled with relative ease. Around 10% of patients have severe asthma requiring long-term treatment with high doses of inhaled or oral corticosteroids combined with adrenergic beta-2 agonists.

Several studies have shown that, despite the availability of therapy, more than half of patients are not well controlled in clinical practice.2-4 Asthma control was recently defined as the extent to which disease manifestations are absent or reduced to a maximum with therapeutic interventions.4 Asthma control has acquired an important role in the management of the disease and is now considered as a reference objective in treatment guidelines. However, there may be discrepancies between physician- and patient-perceived asthma control, and between these latter and the definition of control according to the guidelines. Discrepancies appear to be less pronounced in patients with severe asthma than in those with less severe manifestation.5

Various risk factors associated with poor disease control have been described, including age, educational level, asthma severity and even patients’ knowledge of the disease.2,6,7 Improved awareness of these factors could lead to improved management of asthma.8

The aims of this study were to evaluate the correlation between physician- and patient-perceived control compared with control evaluated according to the criteria of the Spanish Guidelines for Asthma Management (GEMA), and to investigate the factors associated with perception controlled control.

Patients and Methods

A multicenter, observational, cross-sectional study was performed between November 2009 and May 2010 on patients seen in a specialized clinic who met the inclusion criteria. Criteria included patients aged 18 years of age or more, seen in pulmonology and allergy clinics, with spirometry performed within the previous month and persistent severe asthma diagnosed according to the GEMA guidelines; i.e., continuous symptoms during the day, frequent nighttime symptoms, use of rescue medication several times a day, severe limitation of activities, forced expiratory volume (FEV1) $<60$ or $\geq 2$ exacerbations per year. Patients participating in other clinical studies were excluded. The investigators collected study data from the patients’ clinical records and from the information obtained from the patient in the single study visit.

The study was performed in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. The study protocol was approved by the ethics committee of the Hospital Clinic (Barcelona) and reported to the Spanish Agency for Medicinal Products (AEMPS). Informed consent was obtained from all participants.

The principal endpoint was physician- and patient-perceived asthma control, and control according to GEMA criteria (Table 1). In the first case, the patients were asked how they perceived their asthma control, on the basis of their opinion only. They were given 3 choices (controlled, partially controlled or poorly controlled). Physician-perceived asthma control was obtained in a similar fashion. GEMA asthma control criteria (listed in Table 1) were evaluated for each patient and the Asthma Control Questionnaire (ACQ) was self-administered by the patient on the day of the visit,9 taking into account daytime symptoms, nighttime symptoms, limitation of activity and use of rescue medication (short-acting bronchodilators, such as salbutamol) in the previous week, and percent predicted FEV1. The only criteria that referred to the previous year (presence of exacerbations) was obtained from patient interviews and a review of clinical records.10 Only exacerbations in which bronchial obstruction was established clinically and corticosteroids were required were taken into account, as stipulated in the GEMA recommendations. The physician recorded the latest available forced vital capacity (FVC) and FEV1 measurements in the ACQ.

Physicians also completed an ad hoc questionnaire with the following patient variables, and these data were used to complete the patient’s clinical profile and/or were included in the subsequent multivariate analyses: (1) sociodemographic and anthropometric data; (2) physical activity (active: sport or any physical activity $>3$ times a week; moderately active: 2 or 3 times a week; sedentary: none); (3) smoking habit (smoker [defined as smoker in the 30 days prior to the study, including daily smokers], ex-smoker [$< 1$ year, $\geq 1$ year] or never-smoker); (4) asthma clinical history (date of diagnosis, number of visits to emergency room, admissions and unscheduled visits to primary care for asthma in the last year, days with nocturnal awakenings in the last 4 weeks, average use of rescue medication per week, presence and intensity of cough and/or expectoration, concomitant diseases acting as inflammatory stimuli); (5) clinical tests (FVC, FEV1, total IgE, skin prick tests); (6) current asthma treatment (beclometasone/fluticasone/budesonide/formoterol/salmeterol/montelukast/theophyllines/omalizumab/other others); (7) anxiolytic or antidepressant treatment; and (8) additional evaluations (AQLQ quality of life mini-questionnaire,12 questionnaire evaluating knowledge of asthma,13 Hospital Anxiety and Depression [HAD] scale,14 Nijmegen questionnaire [hyperventilation15]).

Statistical Analysis

Qualitative or discrete quantitative variables were summarized using absolute and relative frequencies, while continuous
quantitative variables were described using central tendency and dispersion measurements. The degree of concordance between (a) patient-perceived asthma control and GEMA criteria, (b) physician-perceived asthma control and GEMA criteria and (c) physician-perceived and patient-perceived control was calculated. Differences between controlled patients and uncontrolled patients were evaluated with Chi-squared tests (categorical variables) and the Mann–Whitney–Wilcoxon non-parametric test (continuous variables). The variables with greatest association in the bivariate analysis were included in multivariate logistic regressions in order to determine the variables with a significant independent effect in the perception of asthma control according to patients or physicians. The choice of possible variables was conducted similarly to previous studies. Hosmer and Lemeshow’s goodness-of-fit test was used to determine the total variation explained by the model.

**Results**

**Patient Characteristics and Control According to the Spanish Guidelines for Asthma Management**

A total of 343 patients with a mean age (standard deviation [SD]) of 48.1 (14.7) years were included, of whom one third were women. According to GEMA criteria, only 10.2% of patients were controlled, 27.7% had partial control and 62.1% were poorly controlled. Table 2 shows baseline demographic and clinical data by grades of control. As expected, patients controlled according to GEMA had significantly higher FVC and FEV1 values (Table 2). Moreover, they had higher levels of total IgE (P=.0409). Patients with uncontrolled asthma according to GEMA had a higher body mass index (BMI) (Fig. 1, P=.006) and a more sedentary lifestyle (Fig. 2, P=.016), as well as a tendency toward a higher mean age (48.5 [14.7] vs 44.1 [14.1] years in the controlled asthma subgroup, P=.079).

Omalizumab use, prescribed in 193 of 342 patients, was significantly more prevalent in patients with controlled asthma according to GEMA (71.4%) than in partially controlled patients (63.2%) and those with poor control (49.5%) (P<.005).

No significant association between smoking and asthma control according to GEMA was observed (P=.464).

**Concordance Between Asthma Control According to the Spanish Guidelines for Asthma Management, Patients and Physicians**

According to patients’ perceptions, 42.3% of the population were well controlled, 36.1% had partial control and 21.6% were poorly controlled. According to the physicians, these percentages were 25.7%, 39.7% and 34.6% of patients, respectively.

When the different asthma control criteria were compared, significant differences were observed for all the comparisons made: patient vs GEMA (P<.0001); physician vs GEMA (P<.0001) and patient vs physician (P<.0001). Both patients and physicians overestimated asthma control: in the subgroup of patients with uncontrolled asthma according to GEMA, 35.7% considered themselves to be well controlled (Fig. 3A) and 16.7% were well controlled according to their physician (P<.0001) (Fig. 3B). Of the total sample, 75.8% and 59.3% of patients controlled from the perspective of the patient and the physician, respectively, did not meet the criteria for control according to GEMA.

Patients overestimated asthma control more than physicians: 41.3% of patients who considered themselves controlled were not well controlled according to their physicians (P<.0001) (Fig. 3C).

![Fig. 1. BMI in subgroups defined as asthma control according to GEMA and according to the patient him/herself (controlled/uncontrolled [partially controlled/poorly controlled]). Differences between subgroups according to GEMA criteria were significant (P=.0065) and non-significant according to patient perception (P=.5088).](image-url)
Table 2
Demographic and Clinical Data by Asthma Control According to GEMA Criteria (Controlled/Uncontrolled [Partially Controlled/Poorly Controlled]).

<table>
<thead>
<tr>
<th></th>
<th>Controlled (No.=35, 10.2%)</th>
<th>Uncontrolled</th>
<th>P</th>
<th>Total (No.=343)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>44.1 (14.1)</td>
<td>49.3 (15.0)</td>
<td>48.2 (14.5)</td>
<td>.0786 (A)</td>
</tr>
<tr>
<td>Sex (women)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (%)</td>
<td>26 (74.3)</td>
<td>61 (64.2)</td>
<td>145 (68.1)</td>
<td>.4169 (A)</td>
</tr>
<tr>
<td>Years since diagnosis of asthma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>12.7 (13.7)</td>
<td>13.6 (12.3)</td>
<td>11.8 (12.6)</td>
<td>.2560 (A)</td>
</tr>
<tr>
<td>Smoking habit</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (%)</td>
<td>0 (0.0)</td>
<td>6 (6.3%)</td>
<td>16 (7.5%)</td>
<td>.4640 (A)</td>
</tr>
<tr>
<td>Total IgE (IU/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>628 (962)</td>
<td>437 (509)</td>
<td>373 (523)</td>
<td>.0409 (A)</td>
</tr>
<tr>
<td>FVC, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60%</td>
<td>1 (2.9)</td>
<td>6 (6.3)</td>
<td>31 (14.6)</td>
<td>&lt;.0001 (A)</td>
</tr>
<tr>
<td>60%-80%</td>
<td>2 (5.7)</td>
<td>37 (39.0)</td>
<td>91 (42.7)</td>
<td>130 (37.9)</td>
</tr>
<tr>
<td>&gt;80%</td>
<td>32 (91.4)</td>
<td>52 (54.7)</td>
<td>88 (41.3)</td>
<td></td>
</tr>
<tr>
<td>FEV1, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60%</td>
<td>3 (8.6)</td>
<td>20 (21.1)</td>
<td>80 (37.6)</td>
<td>&lt;.0001 (A)</td>
</tr>
<tr>
<td>60%-80%</td>
<td>5 (14.3)</td>
<td>41 (43.2)</td>
<td>86 (40.4)</td>
<td>132 (38.5)</td>
</tr>
<tr>
<td>&gt;80%</td>
<td>26 (74.3)</td>
<td>34 (35.8)</td>
<td>45 (21.1)</td>
<td></td>
</tr>
<tr>
<td>Skin prick test (positive)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (%)</td>
<td>27 (77.1)</td>
<td>78 (82.1)</td>
<td>158 (74.2)</td>
<td>.4144 (A)</td>
</tr>
</tbody>
</table>

FEV1, forced expiratory volume in first second; FVC, forced vital capacity; GEMA, Spanish Guidelines for Asthma Management; IU, international units.

A Controlled vs uncontrolled.

B Mann–Whitney–Wilcoxon.

C Chi-squared test.

Determinant Factors for Perception of Control by Patients and Physicians

The main factors associated with patient- and physician-perceived lack of control are shown in Tables 3 and 4, respectively (multivariate logistic regression analysis). Other variables tested but not included in either of the two final models were age, sex, level of studies, BMI, time since diagnosis, morning symptoms and treatment with theophyllines.

Five independent factors significantly associated with patient-perceived lack of control were found (Table 3): nocturnal awakenings (P<.0001), a greater perception of breathlessness evaluated according to the Nijmegen questionnaire (P<.0001), more frequent use of rescue medication (P<.0001), more emergency

![Image](image_url)

**Fig. 2.** Level of physical activity in subgroups defined by asthma control according to GEMA (top figure) and the patient (lower figure) (controlled/uncontrolled [partially controlled/poorly controlled]).
room visits in the last year ($P=0.0027$) and greater limitation in activities of daily living ($P=0.0265$). The model was significant and the Hosmer and Lemeshow goodness-of-fit adjustment gave a $P$-value of 0.5080, showing that the analysis explains more than 50% of the variation in patient-perceived asthma control.

In the model for predicting physician-perceived lack of control (Table 4), a total of 6 significant predictive variables were obtained: more frequent use of rescue medication ($P<0.0001$), greater perceived limitation in activities of daily living ($P=0.0002$), FEV1 lower than 80% ($P=0.0031$), no omalizumab treatment ($P=0.0115$),
Identification of potential confounders is critical in the assessment of the effectiveness of asthma control. In a previous study, 

...results observed. This study focuses on the impact of chronic obstructive pulmonary disease (COPD)...

**Results**

The prevalence of asthma control was significantly lower among those with COPD compared to those without COPD. Furthermore, the impact of COPD on asthma control varied by age, sex, smoking status, andcopd severity.

**Discussion**

The results of this study highlight the importance of considering chronic obstructive pulmonary disease (COPD) in the assessment of asthma control. Understanding the specific impact of COPD on asthma control is crucial for developing effective treatment strategies. Further research is needed to explore the potential mechanisms underlying this relationship and to identify strategies for improving asthma control in individuals with COPD.
contrast to another review, no association was found between control and smoking, probably because of differences in the definition of asthma control.

In multivariate analyses, common factors associated with both physician- and patient-perceived lack of control included nocturnal awakenings, frequent use of rescue medication and significant limitation of activities. On the other hand, 4 factors were perceived differently by physicians and patients. When patients’ perception was analyzed, a marked perception of breathlessness and visits to the emergency room in the last year were significant. When physicians’ perception was analyzed, low FEV1 and poor understanding of the biological cause of asthma were significant. Thus, the most important variables in determining the perception of poor asthma control, particularly for patients, are generally related with symptoms and interference in daily life and sleep, while physicians also take lung function into account. With regard to these results, a recent study showed that uncontrolled patients had more catastrophic thinking in the absence of exacerbation, as well as more activity limitation. Thus, the mental component appears to be important in the effective management of uncontrolled asthma. It is interesting to note that neither morning symptoms nor previous exacerbations were taken by the physicians as predictive factors for lack of control. These 2 variables are taken into account in the GEMA classification, but our results suggest that physicians either do not use them in their clinical practice or do not give them the importance they deserve.

Limitations

Since this was an observational, uncontrolled, non-interventional study, there are several limitations inherent in the design, and selection or data bias cannot be ruled out. The amount of information available for each patient and the sample size were limited. Accordingly, it would be of interest to replicate the results in a larger, more diverse group of patients with severe asthma.

Implications for Future Research and Clinical Practice

Control of severe asthma is considered the principal objective of clinical guidelines. In our opinion, the findings of this study have important implications, since they reveal lack of control of asthma in clinical practice and the direct effect this has on patients’ quality of life. Our results also show that, from the patients’ point of view, symptoms should be considered important when evaluating control of severe asthma. In this respect, guidelines should consider the perspective of the patient in order to facilitate physician–patient consensus. Overestimation by physicians must be reduced if better disease control is to be achieved, and raising awareness of the importance of correctly questioning patients about their morning symptoms and exacerbations in the weeks or months before the visit could improve detection of poorly controlled patients. Future studies must also address the cost-efficacy ratio of treatment strategies, based on differences in control achieved by each of those strategies.

Conclusions

In this study, only 1 in 10 patients with severe persistent asthma monitored in specialized clinics are well controlled according to GEMA criteria. Both patients and physicians overestimate control, patients more so, and there is low concordance between perceptions and the GEMA classification. Sedentary lifestyle and obesity are associated with a lack of control according to GEMA, while physicians and patients associate poor control with increased nocturnal symptoms, limitation in activities and use of rescue medication. Our study suggests that a comprehensive approach to patient management, including physical exercise and better eating habits, could improve the control of severe asthma.

Funding

This study was sponsored by Novartis Farmacéutica S.A. This company also funded assistance in scientific writing.

Author Contribution

MCV designed the study and coordinated the study group. All authors participated in the collection of clinical data, reviewed the manuscript and approved the final version.

Conflict of Interests

CP is a member of the International Scientific Advisory Board of Novartis Farmacéutica S.A. and has received research grants from Leti S.A., Uriach S.A. and Chiesi. MCV has received payments from Novartis Farmacéutica S.A. for giving conferences and for consultancy and support for attending scientific meetings. LH, JG and JC are employees of Novartis Farmacéutica S.A., Spain.

Acknowledgements

Our thanks to Emilí Gonzalez-Pérez of the Medical Department of TFS Develop (Barcelona), for providing scientific writing assistance for this article.

References


