Original Article

Changes in Clinical, Pulmonary Function, Quality of Life and Costs in a Cohort of Asthmatic Patients Followed for 10 Years

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ABSTRACT

Few studies have comprehensively assessed the evolution of asthma disease in recent years.

Objectives: To determine changes in morbidity, lung function and quality of life and to establish the impact in terms of cost in a cohort of patients with asthma.

Methods: Prospective, descriptive and realistic study that included 220 asthma patients evaluated 10 years after their inclusion (1994–2004). For all the patients, data for symptoms, lung function, quality of life and financial cost were collected.

Results: There was a decrease in the frequency of health service visits, including: emergency room visits for asthma exacerbations, 0.3 (0.9) versus 0.6 (1) visits per patient per year (P=0.003); a reduction in the severity of the disease, with a greater proportion of patients with mild asthma, 121 (54.8%) versus 94 (42.7%) (P=0.001); a decrease (improvement in quality of life) in the total SGRQ, 30.1 (16.5) versus 37 (19.6) (P<0.001); and reduced total costs, 1464€ (3415.8) compared to 2267€ (4174) per patient/year (P<0.001), mainly due to indirect costs, 617.50€ (2855.9) compared to 1320.10€ (3685.3) per patient/year (P<0.001).

When assessing the changes observed according to asthma severity, no differences were observed between groups.

Conclusions: The evolution of the morbidity and quality of life of asthma patients between 1994 and 2004 are clearly favorable. This improvement provided a significant reduction in the total costs of disease treatment.

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Cambios en la clínica, la función pulmonar, la calidad de vida y los costes en una cohorte de pacientes asmáticos seguidos durante 10 años

RESUMEN

Son escasos los estudios que han evaluado de forma global la evolución de la enfermedad asmática en los últimos años.

Objetivos: Determinar los cambios en la morbilidad, la función pulmonar y la calidad de vida, y establecer el impacto, en términos económicos, de una cohorte de pacientes con asma.

Método: Estudio prospectivo, realista y descriptivo que incluyó 220 asmáticos evaluados a los 10 años de su inclusión (1994–2004). Se recogieron datos clínicos, de función pulmonar, de calidad de vida y de costes económicos.

Resultados: Se observó un descenso en la frecuentación de los servicios sanitarios, entre otros el de las visitas en urgencias por exacerbación asmática, 0.3 (0.9) por 0.6 (1) visitas por paciente/año (P=0.003); una reducción de la gravedad de la enfermedad, con una mayor proporción de pacientes con asma leve, 121 (54.8%) frente a 94 (42.7%) (P=0.001); un descenso (mejoría de la calidad de vida) en la puntuación total del cuestionario de St. Georges, 30.1 (16.5) frente a 37 (19.6) (P<0.001), y una reducción de los costes totales, 1.464€ (3.415.8) por 2.267€ (4.174) paciente/año (P<0.001), fundamentalmente a expensas de los costes indirectos, 617.5€ (2.855.9) frente a 1.320.1€ (3.685.3) paciente/año (P<0.001). Al considerar los cambios observados en función del nivel de gravedad, no se constataron diferencias entre los grupos, mejorando todos por igual.

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Introduction

According to the World Health Organization, asthma is the seventh most prevalent disease in the world, affecting more than 300 million people. It is a chronic respiratory disease that affects all age groups, from newborns to the elderly. In Spain, although there is certain variability depending on the geographical area considered, it is estimated that around 4% of the adult population is affected.\textsuperscript{1,2} In addition, due to causes that have not been well established, said prevalence has increased considerably in recent years, particularly in economically developed countries.\textsuperscript{3} All these logically result in a great consumption of health-care resources. In some countries, the diagnostic and therapeutic management of the disease represents between 1% and 2% of total health-care service expenses.\textsuperscript{4}

These pessimistic numbers are countered by others that are more positive. Recent data on the disease confirm a notable reduction in mortality as well as in frequency of hospital care due to asthma.\textsuperscript{5,6} It is considered that the causes of said reduction could be related with the possible improvement in the attention given by health-care professionals,\textsuperscript{5} the extensive diffusion and the impact of the guidelines for clinical practice in asthma,\textsuperscript{7,8} and particularly by the greater use of inhaled corticosteroids.\textsuperscript{9} In addition to the favorable effects of this group of drugs, we must also take into account the appearance of the new formulations of the last 15–20 years: long-acting β\textsubscript{2}-adrenergic agonists combined in one single inhaler with corticosteroids,\textsuperscript{10} and also leukotriene receptor antagonists.

Nevertheless, there is limited information available on the recent natural history of asthma in standard clinical practice. Specifically, in our setting there are no longitudinal studies in significant patient samples analyzing the predictable changes in morbidity and quality of life over the last 20 years. Along the same lines, there are no studies that have evaluated the impact that the possible changes in morbidity and new treatments could have on the total costs of the disease.

In said context, the cohort of patients known as “asthma in Osona” represents the ideal framework for responding to the questions posed. This group of patients, who have been followed up without interruption by the same group of professionals for twenty years, have provided valuable information in the past about different clinical and economic aspects related to the disease.\textsuperscript{11,12} From this standpoint, the objective of the present study was to determine, in the mentioned patient cohort, the magnitude of the evolutionary changes in their disease in terms of morbidity and mortality, lung function, quality of life and costs during the ten-year period from 1994 to 2004.

Materials and Methods

A prospective, longitudinal, descriptive, realistic study designed in order to determine changes in morbidity and mortality, lung function, quality of life and the costs of a cohort of patients with asthma observed for 10 years (1994–2004). It was carried out in the district of Osona, a semi-rural area in the province of Barcelona (Spain), with some 150,000 inhabitants. The study protocol was approved by the Clinical Research Ethics Committee of the Hospital General de Vic, and all the patients granted their consent to participate.

Conclusions: La evolución de la morbilidad y de la calidad de vida de los pacientes con asma entre 1994 a 2004 años es notoriamente favorable. Dicha mejora se traduce en una importante reducción de los costes económicos ocasionados por la enfermedad.

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the days of work missed and disability were based on the data from
the National Institute of Statistics (Instituto Nacional de Estadística –
INE).18,19 In both phases of the study, the same researcher (AC) was
in charge of interviewing the patients, performing the spirometries
and administering the SGRQ.

Statistical Analysis
A descriptive analysis was completed for the variables collected
from both phases of the study. The values were expressed as means
and standard deviation (SD) or, if necessary, as number of cases with
their percentage. The results of the three asthma severity groups
were compared using the χ² or Fisher’s exact test for the qualitative
variables, or rather with the Kruskal–Wallis test for the quantitative
variables, depending on their distribution. The changes observed
between the two phases were expressed as a difference between
the means and were analyzed with the Wilcoxon test for the quantita-
tive variables; for the qualitative variables, the McNemar test was
used. The Kolmogorov–Smirnov test was used to check whether the
distribution of a variable could be considered normal or not. The
differences with a P-value <.05 were considered statistically signifi-
cant. The information compiled was input after double-checking
and was analyzed in a database with SPSS version 12 software
(SPSS-PC, Chicago, II, USA).

Results
During the 10-year follow-up of the cohort, 21 (6.3%) of the
patients evaluated at the beginning had died. Only one case of death
was caused by a fatal asthma episode. The causes of the remain-
ing deaths were: eight cases of neoplasm (three gastrointestinal,
two pulmonary, one urinary, one bone and one of undetermined
neoplastic etiology); five due to cardiovascular diseases (two cerebrovascular accidents, two refractory heart failures and one
myocardial infarction); four due to severe respiratory infections;
one due to evolved hepatic cirrhosis; another due to biliary sepsis,
and finally one more due to trauma (traffic accident).

Fig. 2 shows the distribution of asthma severity in both phases.
When we compared the proportion of the different levels of severe-
ty between both determinations, we observed that in 151 (69%)
patients there were no changes, 46 (21%) improved and 23 (10%)
worsened. However, when the said changes were considered as
a whole, there was a confirmed improvement in general asthma
severity 10 years later, with a significantly greater proportion of
patients with mild asthma and a reduction of moderate asthma in
phase II compared with asthma in phase I.

Table 1 compiles the results of the 220 (142 [64.5%] women)
patients followed during the 10 years. The comparison between
both phases revealed a general improvement in phase II (2004)
compared with phase I (1994). Thus, among the clinical and mor-
bidity variables for asthma during the previous year, there was
a significant reduction in the number of office visits in primary
care, specialized care and the emergency department as well as the
number of missed work days. At the same time, the use of inhaled
corticosteroids increased significantly and the use of their combi-
nation with long-acting (β₂-adrenergic agonists was introduced: in
2004, 21% of the patients were receiving them, while in 1994 none
received, as the drug was not being commercialized still (data not
shown in Table 1). The total SGRQ score was significantly lower
and, therefore, quality of life improved. In contrast with the earlier
results, there was an observed non-significant decline in the mean
FEV₁. The economic expense analysis showed statistically signifi-
cant changes in the reduction of the total costs, both direct and
indirect. Except for the expenses incurred due to the purchase
of medication and primary-care office visits, both of which increased,
the rest of the different categories that make up the direct costs
(except those caused by blood analyses, which remain unchanged)
were significantly reduced.

With the aim of evaluating the possible different magnitude in
the changes observed between the two phases of the study
according to the level of asthma severity, the sample analyzed was
subdivided into the three levels of severity proposed in the Inter-
national Asthma Consensus of the NIH in 1992: mild, moderate
and severe asthma.14 In order to avoid possible confusion in the
grouping of the cases, we excluded from the following analysis
those patients who had changed in level of severity in phase II.
Therefore, in the end we evaluated with the defined criteria only
those data obtained from the 151 patients who did not change
in asthma severity over the course of the entire study. Table 2
shows in each severity group the difference of the means between
phase I (1994) and phase II (2004) of the variables analyzed in the
151 patients mentioned. The analysis verifies the improvement of
the results of the variables studied in each one of the three lev-
els of severity, with negative values as the general morbidity
and costs declined between the two phases. And, although in some vari-
bles (primary care physician visits, short cycles of corticosteroids,
work absenteeism, SGRQ and indirect costs) there is a tendency
towards a greater reduction (or improvement) in severe asthma,
when compared with mild or moderate asthma, only days of work
absenteeism reached statistical significance.

Discussion
The main contribution of the present study is the confirmation
that the clinical evolution of asthmatic disease in recent years is
notoriously favorable, with a significant reduction in morbidity, an
improvement in the quality of life of the patients and a substan-
tial reduction in total. Also, these changes are independent from
the initial level of severity, even including the severest forms of
the disease. The improvement coincides with the increased use
of inhaled corticosteroids, the introduction of the combinations
of corticosteroids and long-acting (β₂-adrenergic agonists, and
presumably (as they coincide in time) with the publishing of clinical
practice guidelines.14 Furthermore, it is important to highlight the
dimension of the changes observed, which provided a consider-
able reduction (50%) in the rate of emergency department visits
and hospitalizations and a decline of 7 points in the SGRQ, with a
tendency towards being more notable in the moderate and severe
disease types. Consequently, there was a spectacular reduction in
the number of days of work absenteeism associated with asthma.

In general, the results concur with those observed in other
international studies with similar designs.20 Among these are the
so-called “Finnish experience” (The Finnish Asthma Programme),
in which, after the implementation of an ambitious nation-wide
program, they confirmed 10 years after its application (1993–2003) a significant and considerable reduction in morbidity and mortality (particularly in severe exacerbations, hospitalizations and death) and total costs.5

Recent national21,22 and international23 studies have consistently demonstrated that only between 33% and 55% of the patients with asthma are appropriately controlled. A priori, the satisfactory results of our study could go against the widespread opinion of the current insufficient control of asthma. The explanation of the supposed incongruence between both affirmations lies in the fact that, although therapeutic improvements have provided a substantial reduction in morbidity and mortality and an improvement in the quality of life of the patients, they have not been able to promote a less-demanding morbidity, such as that of well-controlled asthma. This circumstance could possibly be related with the limited use of educational programs. A survey carried out in Spain that interviewed more than 1000 physicians who are usually involved in the follow-up of asthma patients, revealed that only 16% of those interviewed declared that a standardized, structured education program was used in their health-care centers.24

Observations made in large patient samples or by using meta-analyses of clinical trials associated the use of long-acting β2-adrenergic agonists with an infrequent but significantly greater risk of death and severe exacerbations.25,26 With said premise, our study should have identified an increase (or at least not show changes) in exacerbations and hospitalizations, as one-fifth of the sample analyzed (21%) were taking them in phase II (2004), compared with phase I (1994) when no patients were. Contrarily, a significant reduction was observed in said parameters, even in the severest patients. These results agree with the growing opinion contrary to the supposed deleterious effect of long-acting β2-adrenergic agonists27 and are in tune with another study recently done in our setting.10

Among the results of the study, we found striking the nonsignificant decline in mean FEV1 (−1.3%) observed when comparing the two phases. This reduction contrasts with the favorable results observed in the rest of the clinical variables analyzed. Nevertheless, it is well-known that the asthmatic population experiences an accelerated progressive loss in lung capacity compared with the non-asthmatic population.10 This deterioration is only partially prevented by corticosteroid treatment, which evidently differs with the beneficial action that said drugs have on clinical variables or indicators.28 On the other hand, a greater loss in lung function has been associated with patients who suffer frequent asthma exacerbations, a circumstance attributed to the phenomenon of bronchial remodeling that accompanies the exacerbation.29 Along this line, we should indicate that our study, in agreement with others,20 verified a non-significant tendency in the mild asthma group towards preserving FEV1 (0.3%) compared with the decline observed in those with moderate and severe asthma (−4.2 and −1.1%, respectively). Moreover, these are groups that presented a greater tendency towards exacerbations (visits to emergency and hospitalization) due to asthma.

The analysis of the economic data of the study revealed that, in agreement with the lower morbidity and particularly the decline in hospital care, the total costs decreased significantly. The mean of the total cost per patient registered in 2004 represented a decrease of 35% over the average of 1994. These data are equivalent to that
observed in the Finnish experience, where the application of their national program provided a reduction of 36% in total costs.5 The mean total cost in our study was 1464.40€, which also does not differ substantially from another study recently done in a Spanish sample with 627 patients (ASMACOST study),30 which established this amount at 1533€. The reduction in total costs observed in the present study came from both the direct as well as the indirect costs. Regarding the direct costs, although there was a statistically significant increase in the expense caused by the purchase of drugs and primary care office visits in 2004 compared to 1994, the decrease in other direct costs—particularly those related with hospitalizations, emergency department visits and specialized care—resulted in a significant reduction in the sum of the direct costs. Along the same lines, the decline in the number of days of work missed provided a significant and considerable reduction, somewhat more than half of the indirect costs. These results are particularly relevant as some pharmacoeconomic studies usually present partial cost analyses, sometimes elaborated by the health-care administrations themselves, excluding from the evaluation the indirect costs and those related with the frequency of health-care required. It is an improper procedure because in this manner the impact provided by the efficiency of the medication for better controlling a disease, as happens in asthma, cannot be evaluated in the dimension that cost analyses require. Other studies show results that are equivalent to those of this present study, also finding an increase in the costs for medication, but a reduction in direct and total costs.5

As for the potential limitations of the study, the quality of the results could be questioned as they are obtained from a cohort with 33.3% of lost cases. Nevertheless, said loss is within reason as it is a study carried out over a prolonged period of time. In addition, this percentage is even less than those of other series with similar designs.20,31 Therefore, in our opinion, the loss of cases in this study does not limit its validity or the extent of its conclusions.

In short, the present study covers a lack of local information about the natural history of asthma in actual clinical practice situations. The results demonstrate a favorable evolution of the patients with asthma in our setting in recent years. This improvement is supported by a considerable reduction of the frequency of healthcare resources used, an important increase in the quality of life of the affected patients and, consequently, a notable reduction in total costs caused by asthma. Even though this observation can probably be extrapolated to the rest of the Spanish asthmatic population, it would be recommendable to analyze data from studies with similar designs and objectives from different geographical locations of our country.

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### References


