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Effectiveness of a Specific Program for Patients With Chronic Obstructive Pulmonary Disease and Frequent Exacerbations

Juan José Soler,[a] Miguel Ángel Martínez-García,[a] Pilar Román,[b] Rosa Orero,[b] Susana Terrazas,[b] and Amparo Martínez-Pechuán[b]

[a]Unidad de Neumología, Servicio de Medicina Interna, Hospital General de Requena, Requena, Valencia, Spain.
[b]Servicio de Medicina Interna, Hospital General de Requena, Requena, Valencia, Spain.

OBJECTIVE: Patients with chronic obstructive pulmonary disease (COPD) and a history of frequent exacerbations are a target population of particular interest from both a clinical and an economic standpoint. The objective of this study was to evaluate the effectiveness of a program designed specifically to manage patients in this subgroup.

PATIENTS AND METHODS: This was a 1-year randomized controlled trial designed to compare the effectiveness of a specific program (SP) with that of conventional management (CM) in a group of patients with a high frequency of exacerbations (3 or more per year). Within-group and between-group comparisons were carried out for a number of variables related to the patients' medical care, dyspnea, health-related quality of life (HRQL), inhaler technique, and pulmonary function.

RESULTS: A total of 26 patients were enrolled in the study (all men). The mean (SD) age was 73 (8) years, and mean forced expiratory volume in 1 second (FEV_1) expressed as a percentage of the reference value was 43% (15%). Exacerbations requiring hospital care (emergency department visits and/or admission) decreased in both groups: by 24.4% (*P* not significant) in the CM group and 44.1% (*P*=.061) in the SP group. Hospital admissions decreased 73.3% in the SP group and increased 22% in the CM group (*P*<.001). While length of hospital stay decreased 77.3% in the SP group, this figure almost doubled in the CM group (*P*=.014). Dyspnea, HRQL, and inhaler technique improved in both groups. FEV_1 fell by 46 mL/year in the CM group and increased 10 mL/year in the SP group (*P* not significant).

CONCLUSIONS: The use of a simple program to manage selected patients with a history of frequent exacerbations produces a significant reduction in the number of hospital admissions, an improvement in HRQL, and may improve prognosis.

Key words: *Chronic obstructive pulmonary disease. Exacerbations. Hospitalization. Education.*

Eficacia de un programa específico para pacientes con EPOC que presentan frecuentes agudizaciones

OBJETIVO: Los pacientes con enfermedad pulmonar obstructiva crónica que presentan frecuentes agudizaciones (AEPOC) constituyen una población diana de especial interés, tanto desde el punto de vista clínico como económico. El objetivo del estudio es evaluar la eficacia de un programa específico (PE) dirigido a este subgrupo de enfermos.

PACIENTES Y MÉTODOS: Se ha realizado un estudio prospectivo, aleatorizado y controlado de un año de duración, en el que se ha comparado la eficacia del PE frente al tratamiento convencional (TC) en un grupo de pacientes con exacerbaciones frecuentes (3 o más AEPOC al año). Se efectuaron comparaciones intragrupo e intergrupo en diversos parámetros asistenciales, disnea, calidad de vida relacionada con la salud (CVRS), técnica inhalatoria y función pulmonar.

RESULTADOS: Se incluyó en el estudio a 26 pacientes (todos varones), con una edad media (± desviación estándar) de 73 ± 8 años y volumen espiratorio forzado en el primer segundo, en porcentaje del valor de referencia, del 43 ± 15%. Las exacerbaciones que precisaron atención hospitalaria (visitas a urgencias y/u hospitalizaciones) disminuyeron en ambos grupos: un 24,4% (p = no significativo) en el grupo TC y un 44,1% (p = 0,061) en el grupo PE. Las hospitalizaciones se redujeron un 73,3% en el grupo de intervención, mientras que se incrementaron un 22% en el TC (p < 0,001). Los días de hospitalización disminuyeron un 77,3% en el PE, mientras que aumentaron casi el doble para el TC (p = 0,014). La disnea, la CVRS y la técnica inhalatoria mejoraron en ambos grupos. El volumen espiratorio forzado en el primer segundo presentó un descenso de 46 ml/año en grupo TC, mientras que se incrementó 10 ml/año para el grupo PE (p = no significativo).

CONCLUSIONES: El empleo de un programa sencillo, dirigido a pacientes seleccionados con exacerbaciones frecuentes, comporta una reducción significativa del número de las hospitalizaciones, mayor CVRS y quizá mejor pronóstico.

Palabras clave: *Enfermedad pulmonar obstructiva crónica. Exacerbaciones. Hospitalización. Educación.*

Introducción

Exacerbations play a very important role in the natural history of chronic obstructive pulmonary disease (COPD) and have a clear influence on the health-related quality of life (HRQL) of patients with this disease.[1] Since exacerbations place a heavy burden on the health

Correspondence: Dr. J.J. Soler.
Unidad de Neumología. Servicio de Medicina Interna.
Hospital General de Requena.
Paraje Casablanca, s/n. 46430 Requena. Valencia. España.
E-mail: jjsoler@telefónica.net

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care system, their economic impact is high.[2,3] Finally, they even represent an adverse prognostic factor.[4] On average, patients with COPD have between 1 and 4 exacerbations per year.[5] However, the distribution and severity of these episodes varies between patients. In the ISOLDE trial, which prospectively followed up patients with moderate to severe COPD for 3 years, up to 20% of patients had no exacerbations.[6] In an outpatient study of COPD patients with less severe disease and milder exacerbations, Miravitlles et al[5] reported that 31% of patients had 3 or more exacerbations a year. In a series of patients managed in a respiratory clinic setting, we found that 60% of patients experienced no exacerbations requiring hospital care while a small subgroup (10%-12%) presented frequent exacerbations that gave rise to a hospital visit.[2] It is our opinion that this group of frequent exacerbators constitutes a target population. Around 60% of all hospital visits (both emergency department visits and hospital admissions) were generated by this small group of patients,[2] who are individuals with advanced lung disease characterized by high comorbidity, poor HRQL,[7] accelerated lung function decline,[8] and a poor prognosis.[4]

From a strategic standpoint, it would appear necessary to reduce the frequency of exacerbations, and several therapeutic options have been shown to be useful in achieving this goal. Pharmacological treatments that reduce exacerbations by 25% to 30% include inhaled corticosteroids,[6] long-acting bronchodilators,[9,10] and combinations of long-acting β_2-agonists and inhaled corticosteroids.[11] Antioxidants such as N-acetylcysteine[12] and pulmonary rehabilitation[13] are 2 other treatments that have been associated with reductions in the exacerbation rate, although there is less evidence supporting the use of these last 2 treatments. There is also some evidence for the effectiveness of the influenza vaccination[14] and patient education, although there is still no consensus on the latter.[14-16] Combined coordinated use of all of these resources in conjunction with strategies aimed at optimizing and maximizing preventative treatment could potentially be of great use, particularly in the subgroup of patients at higher risk for exacerbations. The objective of this study was to evaluate the effectiveness of a program designed specifically to manage COPD patients with a history of frequent exacerbations comprising an educational program and regular clinical monitoring at a specialized respiratory clinic.

Patients and Methods

Study Population

This was a 1-year prospective randomized controlled trial that compared the usefulness of a specific program (SP) with that of conventional management (CM) in COPD patients with a history of frequent exacerbations. Patients with COPD were considered to be frequent exacerbators if they had had 3 or more exacerbations requiring hospital treatment (emergency department visits and/or hospitalization) during the year preceding the study. An exacerbation was defined as any sustained increase from baseline in respiratory symptoms requiring a change in regular medication and generating the need for medical attention.[17] The COPD diagnosis was based on the presence of a smoking history (current or prior smoker) of at least 20 pack-years and of a mostly irreversible airflow limitation defined as a postbronchodilator ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) of less than 70%. Excluded from the trial were patients who had been previously diagnosed with bronchial asthma, bronchiectasis, cystic fibrosis, or upper airway limitation, and individuals with bronchiolitis secondary to systemic diseases. All the patients treated in our clinic who fulfilled the definition of frequent exacerbator during the course of 2001 were enrolled.

Specific Program

The key components of the SP were a schedule of monthly clinical visits to a specialized clinic and a short educational program. At each monthly visit, in addition to their personal medical consultation, patients attended a group educational session led by the nursing team (4-6 patients). Patients and their families also attended an informative session that included an explanation of COPD and recommendations on how to manage the disease (anti-smoking advice, use of inhalers, exercise, nutrition, sleeping habits, etc). The educational program was supported by specially designed printed material.[18] Patients were not instructed in self-management of exacerbations, and no self-management plan was provided.

Pharmacological treatment was standardized; all the patients received ipratropium bromide regularly, long-acting inhaled β_2-adrenergic agonists, high doses of inhaled corticosteroids (1000 µg/day of fluticasone), and salbutamol ad libitum. Both the choice of the long-acting β_2-agonist (formoterol or salmeterol) and the prescription of a combination treatment (N-acetylcysteine, oral theophyllines or other drugs) were decided on a patient-by-patient basis by the attending specialist. None of the patients received maintenance oral corticosteroids, and none of them underwent pulmonary rehabilitation, domiciliary noninvasive mechanical ventilation, or lung reduction surgery. All current smokers were enrolled in a smoking cessation program. The treatment of any exacerbations that occurred during the 1-year study period was not standardized, all such treatment being left to the judgment of the attending physician in each case.

Conventional Management

The patients assigned to the CM group received the same treatment as the patients in the SP group. However, in the CM group, consultation with a specialized physician only took place once every 3 months. Furthermore, these patients did not attend the educational program, though did receive information about COPD and how to manage the disease, including nutritional advice and insistent recommendations about the need for physical exercise (a daily walk). They received instruction on proper inhaler technique at the first visit.

Study Variables

In stable situation (4 weeks without exacerbation), prior to randomization, and after 1 year of follow-up, the following data were collected prospectively: age, smoking history, baseline symptoms, comorbidity, and HRQL. Dyspnea was assessed using a modified Medical Research Council scale.[19]

HRQL was evaluated using the Spanish version of the St George's Respiratory Questionnaire.[20] Comorbidity was quantified using the Charlson index.[21] The following tests were carried out for all patients: baseline carbon monoxide pulse oximetry (Micro CO meter, Micro Medical Limited, Rochester, United Kingdom), a simple nutritional assessment, electrocardiogram, evaluation of inhaler technique, forced spirometry with a bronchodilator test, and arterial blood gas analysis. Body mass index was calculated by dividing the patient's body weight (kg) by the square of their height (m^2). FEV_1 and FVC were measured by forced spirometry (Vmax Spectra, SensorMedics Corporation, Yorba Linda, California, USA) in accordance with the guidelines of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR).[22] FEV_1 and FVC results are expressed as a percentage of reference values for an adult population.[23] Arterial blood gas analysis was performed on resting patients using the methodology recommended by SEPAR.[24] Inhaler technique was reviewed in each individual and the use of each type of inhaler used was assessed separately. Each step in the process was scored from 0 to 2 according to whether the reviewer considered that the patient's execution of the step was deficient or omitted (0 points), acceptable (1 point), or satisfactory (2 points). The maximum scores were 12 points (6 steps assessed) for canister inhalers with a spacer device and 8 points (4 steps assessed) for dry powder inhalers.

The number of COPD exacerbations dealt with in our hospital during the 12-month period before the study was calculated using the hospital database. The following data were recorded prospectively: primary care physician consultations; visits to our clinic; visits to the hospital's emergency department; hospital admissions; length of stay in hospital; and admissions to the intensive care unit.

Statistical Analysis

The patients selected were assigned randomly to either the SP group or the CM group. In order to create 2 groups of similar severity, a balanced randomization method was used based on 3 parameters: FEV_1, age, and baseline PaO_2. Health care visits during the 1-year study were adjusted by month of enrollment. The denominator was 12 for patients who completed 12 months of follow-up. In the case of patients who died, the denominator corresponds to the number of months the patient lived after random assignment to a group. The number of health care visits generated during the previous year (the baseline situation) was adjusted to 12 months in all cases. The χ^2 test was used to compare proportions at baseline, and the Mann-Whitney U test to compare quantitative variables. The Wilcoxon test was used to analyze within-group paired comparisons (baseline and end-point). We used a repeated measures analysis to analyze differences in course between groups. Mauchly's sphericity test was used to determine whether the variance-covariance matrix was circular. As the sample was small, a correction was made in the degrees of freedom of the numerator and denominator to validate the univariate F statistic. An alpha error of 0.05 was assumed. The statistical analysis was carried out using the SPSS statistical package, version 11.5 for Windows (SPSS Inc, Chicago, Illinois, USA).

Results

Baseline Patient Characteristics

A total of 124 patients with COPD required medical attention in our hospital and generated 273 hospital visits. Of the 124 cases, 38 (30.6%) had 3 or more severe COPD exacerbations. These 38 patients generated over 170 hospital visits and accounted for 62.3% of all the visits during that year. Seventy-one (41.8%) of these visits gave rise to an admission (accounting for 59.2% of all admissions for COPD exacerbation). Nine patients (23.7%) died before being selected and 3 (7.9%) died before randomization. Altogether, 26 patients (20.9%) were included in the

TABLE 1
Baseline Patient Characteristics*

	Groups		
	CM (n=13)	SP (n=13)	*P*
Age, y	73 (9)	74 (7)	NS
Smoking, n (%)			
Ex-smokers	12 (92.3)	10 (76.9)	NS
Current smokers	1 (7.7)	3 (23.1)	NS
Pack-years	92 (66)	67 (52)	NS
FACO, ppm	2.3 (1.0)	4.2 (3.9)	NS
BMI, kg/m^2	26.8 (4.5)	26.9 (6.5)	NS
Charlson index	2.8 (1.1)	2.6 (1.0)	NS
Dyspnea (MRC)	2.8 (0.9)	2.6 (1.0)	NS
PB FEV_1, mL	897 (333)	920 (272)	NS
PB FEV_1%	43.3 (16.9)	42.2 (14.3)	NS
FVC, mL	2070 (437)	2051 (672)	NS
FVC%	70.0 (15.6)	74.0 (24.1)	NS
PaO_2, mm Hg	62 (7)	60 (10)	NS
PaO_2/FiO_2	293 (35)	263 (49)	NS
$PaCO_2$, mm Hg	42 (8)	51 (13)	NS

*Quantitative variables are expressed as means (SD) unless otherwise indicated as number of cases (percentage). CM indicates conventional management group; SP, specific program group; NS, not significant; FACO, fractional alveolar concentration of carbon monoxide; BMI, body mass index; MRC, the Medical Research Council dyspnea scale; FEV_1, forced expiratory volume in 1 second; PB, postbronchodilator; FVC, forced vital capacity; and FiO_2, fraction of inspired oxygen.

TABLE 2
Initial Drug Therapy*

	TC (n=13)	PE (n=13)	*P*
Short-acting inhaled bronchodilators			
Ipratropium bromide	13 (100)	13 (100)	NS
Salbutamol, ad libitum	13 (100)	13 (100)	NS
Long-acting inhaled bronchodilators	13 (100)	13 (100)	NS
Salmeterol	8 (61.5)	6 (46.2)	NS
Formoterol	5 (38.5)	7 (53.8)	NS
Oral theophyllines	7 (53.8)	8 (61.5)	NS
Inhaled corticosteroids			
Fluticasone	13 (100)	13 (100)	NS
Combination herapy			
Fluticasone/salmeterol	8 (61.5)	5 (38.5)	NS
N-acetylcysteine	11 (84.6)	11 (84.6)	NS
Diuretics	4 (30.8)	3 (23.1)	NS
Home oxygen therapy	7 (53.8)	9 (69.2)	NS
Antidepressants	3 (23.1)	1 (7.7)	NS
Influenza vaccination	13 (100)	13 (100)	NS

*Data are expressed as number of cases (percentage).
CM indicates conventional management group; SP, specific program group; NS, not significant.

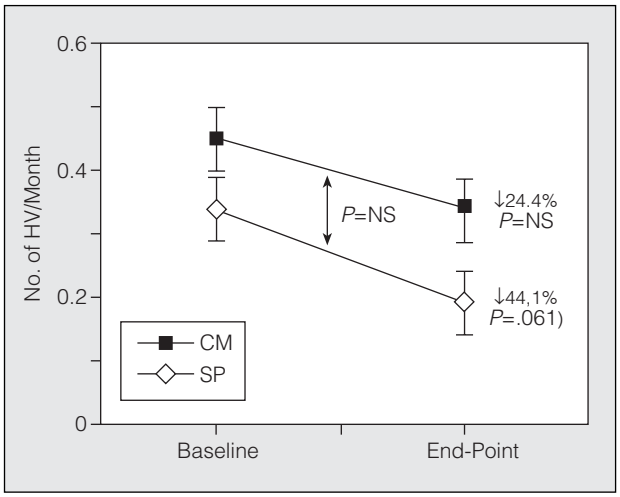

Figure 1. Number of hospital visits (HV) per month. CM indicates conventional management group; SP, specific program group; and NS, not significant.

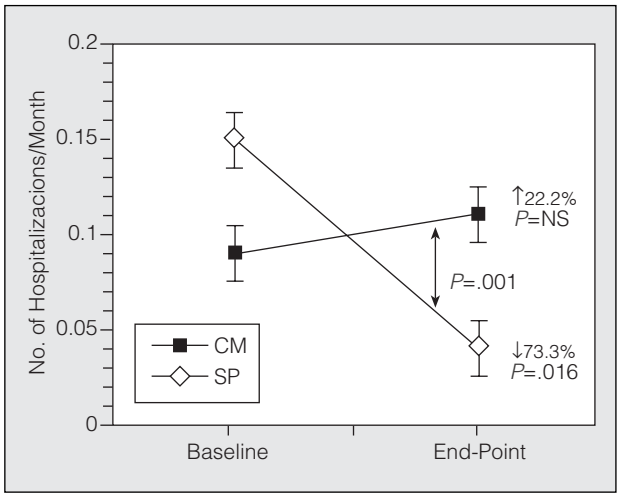

Figure 2. Number of hospital admissions per month. CM indicates conventional management group; SP, specific program group; NS, not significant.

trial. All the participants were men, and the mean (SD) age was 73 (8) years. Table 1 shows the baseline patient characteristics. Both groups (SP and CM) were similar with respect to the main variables studied. Pharmacological therapy was similar in both groups (Table 2).

Health Care Visits

Table 3 shows the number of health care visits adjusted by month. The number of hospital visits (both emergency department visits and admissions) declined in both groups, although no significant differences between the 2 groups were observed (Figure 1). In the CM group, the mean number of visits decreased by 24.4% to 0.34 (0.28) from 0.45 (0.45); *P*=not significant (NS). In the SP group, the mean number decreased by 44.1% from 0.34 (0.24) to 0.19 (0.28); *P*=.061. Emergency department visits also tended to decrease in both groups, although not significantly. However, significant differences between the groups were observed in both the number of hospital admissions (*P*<.001) and the number of inpatient bed-days (*P*=.014), with a marked reduction in both variables for the patients in the SP group. Among patients in the SP group, the mean number of admissions per month decreased by 73.3% from 0.15 (0.06) to 0.04 (0.09); *P*=.016. In the CM group, the number of admissions increased 22.2% from 0.09 (0.07) to 0.11 (0.11); *P*=NS) (Figure 2). The mean number of inpatient bed-days per month decreased in the SP group by 77.3% from 0.97 (0.61) to 0.22 (0.60); *P*=.012), while this figure almost doubled in the CM group, going from 0.57 (0.50) to 1.21 (1.80); *P*=NS. The number of visits to a primary care physician decreased in both groups, and no statistically significant between-group differences were observed. Visits to the specialized respiratory clinic increased, particularly in the SP group (*P*=.002). During the study period, there was only 1 admission to the intensive care unit, which occurred in the CM group. Six patients (23.1%) died during the 1-year study, 3 in each group (*P*=NS).

Clinical Course

Table 4 shows how the disease evolved in these patients over the course of the study. A decrease in

TABLE 3
Number of Hospital Visits (HV) Adjusted by Month*

	CM			SP			*P*‡
	Preceding Year	Study Period	*P*†	Preceding Year	Study Period	*P*†	
HV/month	0.45 (0.45)	0.34 (0.28)	NS	0.34 (0.24)	0.19 (0.28)	.061	NS
No. EVWA/month	0.36 (0.44)	0.23 (0.21)	NS	0.19 (0.21)	0.15 (0.21)	NS	NS
A/month	0.09 (0.07)	0.11 (0.11)	NS	0.15 (0.06)	0.04 (0.09)	.016	<.001
Days H/month	0.57 (0.50)	1.21 (1.80)	NS	0.97 (0.61)	0.22 (0.60)	.012	.014
PCP visits/month	0.60 (0.82)	0.11 (0.16)	.050	0.30 (0.34)	0.07 (0.07)	.040	NS
OPC/month	0.24 (0.10)	0.37 (011)	.021	0.27 (0.09)	0.65 (0.18)	.004	.002

*CM indicates conventional management group; SP, specific program group; HV, hospital visits (both emergency department visits and hospitalizations); EVWA, emergency department visits without admission; A, hospital admissions; PCP, primary care physician; OPC, outpatient pulmonology consultations; and NS, not significant.
†Significance level for the within-group paired comparison.
‡Significance level for the between-group comparison.

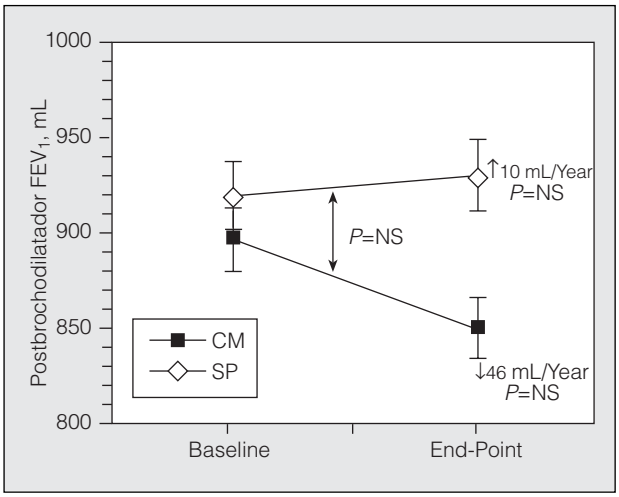

Figure 3. Evolution of postbroonchodilatador FEV_1 during the study. CM indicates conventional management group; SP, specific program group; NS, not significant.

dyspnea and a clinically significant improvement in SGRQ total score was observed in both groups. However, no significant differences between the groups were found. The patients in the SP group improved significantly in the symptoms domain (*P*=.018) while, paradoxically, patients in the CM group improved in the activity domain (*P*=.020). Inhaler technique improved to some degree in both groups, but the change was not significant. Patients in the SP group who used a pressurized cartridge inhaler with spacer went from baseline scores for technique of 7.8 (1.5) to 9.8 (3.9) out of a maximum score of 12 points (*P*=NS), while those in the CM group went from 6.7 (2.4) to 8.5 (1.7) points (*P*=NS). Among patients in the SP group who used a dry powder inhaler, score for technique improved from 5.1 (1.5) to 7.0 (1.8) out of a maximum of 8 points (*P*=.058), while the score for those in the CM group went from 4.5 (2.8) to 6.6 (1.3) points (*P*=NS).

Changes in Lung Function

Table 5 shows the change over the course of the study in the lung function parameters monitored. The only significant between-group differences observed were in the ratio of PaO_2 to fraction of inspired oxygen (FIO_2). While a marked decline in the ratio of PaO_2 to FIO_2 was observed among the patients in the CM group (*P*=.08), in the SP group this ratio tended to increase, although the change was not significant (*P*=NS). $PaCO_2$ increased in the CM group (*P*=.043), and varied only very slightly in the SP group, but no significant differences between the 2 groups were found in this parameter. Although not significant, the changes in FEV_1 after bronchodilation should be reported. In the CM group the results show a mean decline of 46 mL/year (from 897 [333] mL to 851 [232] mL; *P*=NS). By contrast, the results in the SP group show a mean increase of 10 mL/year (from 920 (272) mL to 930 [355] mL; *P*=NS) (Figure 3).

TABLE 4
Clinical Course*

	CM			SP			P‡
	Baseline	End-Point	*P*†	Baseline	End-Point	*P*†	
Total SGRQ,	65.3 (18.0)	53.3 (13.1)	.036	54.7 (12.2)	38.7 (14.7)	.028	NS
Symptoms	59.6 (21.1)	46.0 (18.3)	NS	48.6 (19.4)	25.4 (9.0)	.018	NS
Impact	53.8 (17.9)	48.4 (15.3)	NS	50.8 (18.3)	40.3 (21.3)	NS	NS
Mobility	84.4 (18.9)	76.4 (14.9)	.020	76.4 (15.6)	70.3 (24.5)	NS	NS
Dyspnea (MRC)	2.70 (0.82)	2.30 (1,41)	NS	2.56 (0.72)	1.89 (1.16)	.034	NS

*CM indicates conventional management group; SP, specific program group; SGRQ, St George's Respiratory Questionnaire; MRC, the Medical Research Council dyspnea scale; NS, not significant.
†Significance level for the within-group paired comparison.
‡Significance level for the between-group comparison.

TABLE 5
Evolution of Lung Function*

	CM			SP			P‡
	Baseline	End-Point	*P*†	Baseline	End-Point	*P*†	
BMI, kg/m^2	27.5 (5.2)	28.0 (5.6)	NS	28.2 (6.9)	26.9 (6.9)	NS	NS
PB FEV_1, mL	897 (333)	851 (232)	NS	920 (272)	930 (355)	NS	NS
FVC, mL	2070 (437)	1871 (511)	NS	2051 (672)	1926 (679)	NS	NS
FEV_1/FVC	42.3 (12.1)	46.2 (4.8)	NS	46.8 (12.0)	48.3 (9.3)	NS	NS
PaO_2, mm Hg	61.5 (7.3)	57.2 (9.8)	NS	59.6 (10.3)	63.4 (13.4)	NS	NS
PaO_2/FiO_2	293 (35)	243 (75)	.080	263 (49)	273 (64)	NS	.029
$PaCO_2$, mm Hg	41.5 (7.8)	47.7 (10.1)	.043	51.4 (12.9)	49.9 (16.6)	NS	NS

*Data are expressed as means (SD). CM indicates conventional management group; SP, specific program group; BMI, body mass index; PB, postbronchodilator; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; FiO_2, fraction of inspired oxygen.
†Significance level for the within-group paired comparison.
‡Significance level for the between-group comparison.

Discussion

Our study demonstrates the effectiveness of a SP of therapeutic intervention targeting COPD patients with a history of frequent exacerbations. This therapeutic program, the essential components of which are basic educational support and regular clinical monitoring, can substantially reduce the frequency of severe COPD exacerbations, and in particular episodes that lead to hospitalization. Among the patients in the SP group, hospital admission decreased by just over 70%, and the number of inpatient bed-days by around 80%. The reduction in the number of COPD exacerbations was associated with a clinically significant improvement in HRQL, especially in the symptoms domain, and a trend towards stabilization of lung function decline was observed. Although this trial should be seen as a pilot study, we believe that these results point the way towards an interesting approach to the management of COPD patients with important clinical, financial and perhaps even prognostic implications.

Several studies have evaluated the effectiveness of programs, especially those based on home care, designed to reduce the number or length of hospital stays[25-29] but the results are inconsistent. In the largest study, 301 patients with COPD were randomly assigned to 3 groups and received either home care provided by respiratory nurses or home care provided by nonspecialist nurses, or were managed conventionally.[25] The home care program was associated with higher costs, and produced no appreciable improvement in the patients' health. In another study, patients receiving home care visited their primary care physician more often and were prescribed more medication.[26] No differences were found in number of hospital admissions, exercise tolerance, or HRQL. These results indicate that home care programs in unselected patients do not reduce the need for hospitalization. However, the results may be different when such programs include multidisciplinary treatment and, more importantly, when they target selected patients. Haggerty et al[27] reported the results of a program in which 17 patients with severe COPD and a history of several prior hospitalizations received multidisciplinary treatment in conjunction with home care. The number of hospital admissions, the length of hospital stays, and the number of emergency department visits were all significantly lower compared to the year before the study. The net financial saving per patient was estimated to be US $330. However, this was not a controlled study. In a recent trial, Poole et al[28] compared 16 patients with these characteristics and a control group. In the group of patients who received education, training, and home care, the number of inpatient bed-days decreased significantly and HRQL improved. The number of hospital admissions declined in both groups. Our results also support the usefulness of implementing this kind of specific intervention in selected patients with COPD, in this case, frequent exacerbators. In our study the number of exacerbations decreased in both groups (Figure 1), but the reduction among patients in the SP group was appreciably greater, particularly in hospital admissions (Figure 2). Admissions were reduced by up to 73.3% and inpatient bed-days by up to 77.3% among the patients who participated in the specific intervention program. By contrast, inpatient bed-days almost doubled in the control group. HRQL also improved significantly in the intervention group. Total SGRQ score decreased on average by 16 points among the patients in the SP group, a figure that amply exceeds the 4-point threshold considered clinically significant.[30] The most satisfactory results were observed in the symptoms domain, probably because the patients in this group experienced an appreciable improvement in the level of dyspnea.

The influence that a reduction in the incidence of severe COPD exacerbations could have on mortality is of particular interest. A group of British researchers recently demonstrated that patients who had 3 or more COPD exacerbations per year experienced a greater decline in lung function.[8] A reduction in this kind of exacerbation could, therefore, have beneficial effects. While we did not observe any significant between-group differences, the mean decline in FEV_1 among patients in the control group was 46 mL/year. By contrast, FEV_1 in the SP group, rather than declining, improved by around 10 mL/year. Although the difference was not statistically significant, it does suggest a very interesting hypothesis in that it highlights the possibility of improving prognosis by reducing the incidence of severe exacerbations. Similarly, it was recently reported that the frequency and severity of exacerbations are significantly and independently related to mortality in patients with COPD.[4] This effect is appreciably greater among frequent exacerbators because the risk of death in this group of patients is 4 times that of patients with no history of exacerbations.[4] On the basis of this premise, we could expect a beneficial effect on mortality in our series, but there were 3 deaths (23.1%) in both the specific intervention group and the control group. In the series of cases studied by Poole and coworkers,[28] there were 3 deaths in the control group and 1 in the intervention group, although the differences were not statistically significant. Since the sample size was small and the follow-up period was short in both of these studies, we cannot rule out the possibility that these factors may have had a beneficial effect on survival. Further studies focusing on this interesting line of study are needed.

In our opinion, the benefits observed with the SP may be due to either the increase in the frequency of health care visits or to the educational component of the intervention. However, the study design does not allow us to ascertain which of these 2 factors was more influential. The control group was assessed with the same rigor as the intervention group; in both groups patients were given information about the disease and pharmacological treatment was optimized. However, the greater frequency of visits in the SP group could have resulted in a better adjustment of treatment or better intervention in the event of an exacerbation. It

was recently demonstrated that early action to manage COPD exacerbations can reduce the consequences associated with these episodes.[31] Increasing the frequency of visits could, purely from the point of view of timing, facilitate the early detection of more exacerbations and these episodes could then be averted by timely and more precise therapeutic measures. In the control group, 3 exacerbations were detected in the course of scheduled visits, while in the intervention group 6 exacerbations were detected at regular monthly visits. This possible beneficial effect, although present, appears to be slight and, in our opinion, would not explain the overall benefit observed. In fact, the differences were not statistically significant.

The role of educational interventions in COPD has, for some years, been a source of some debate. A recent Cochrane review[16] of 8 randomized controlled trials concluded that there is currently insufficient evidence to draw conclusions or make recommendations on this topic. The reasons given included the variation in the patients and outcome measures that have been studied. Once again, the selection of participants may have influenced the results obtained. Bourbeau et al,[15] in a large study of 191 patients with severe COPD and a history of at least 1 hospitalization for exacerbation during the previous year, reported a 39.8% reduction in hospital admissions and a significant decline in visits to both the emergency department and to primary care physicians. The number of hospital admissions also declined in the control group by over 20%. They studied the use of an intensive educational intervention administered over a 2-month period characterized by weekly sessions and a self-management program. The patients in our study were not given a self-management plan that could have reduced or averted exacerbations through early treatment. Consequently, we believe that the benefit obtained must be related to other aspects of our educational intervention. The patients' inhaler technique improved. However, the improvement was similar in both groups. The improvement observed in the intervention group could also be attributed to better compliance or a reduction in therapeutic errors. Unfortunately, these variables were not studied either by us or by Bourbeau and colleagues.

Finally, we should note the limitations that affected the present trial. In the first place, the sample was small. In an effort to correct this problem we selected all patients who fulfilled the criteria of frequent exacerbators. However, as noted earlier, the final sample was small and mortality was unusually high. Further research, probably taking the form of multicenter trials enrolling a larger number of patients, is required to verify our findings. Furthermore, it may perhaps be surprising that long-acting anticholinergic agents and pulmonary rehabilitation were not used in this trial, since both these therapeutic approaches have been shown to reduce the number of exacerbations in patients with COPD.[10,13] Tiotropium bromide was not used because this drug was not available in Spain at the beginning of the trial. Respiratory rehabilitation was initially planned. However, in the event it was not possible to offer these patients rehabilitation because of logistical problems in the hospital's rehabilitation clinic. This is, unfortunately, an all too common situation in Spain. In a trial undertaken in Barcelona, just over 85% of patients admitted for exacerbations had not participated in any rehabilitation program during the previous year.[32]

In conclusion, we believe that the use of programs specifically targeting COPD patients with a history of frequent exacerbations is highly recommendable. The use of a simple program, such as the one we propose, produces important benefits, including a reduction in hospital admissions and better HRQL, and may improve prognosis.

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