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Comparison of Fenspiride with Beclomethasone as Adjunctive Anti-Inflammatory Treatment in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Objective: This study aimed to compare the clinical efficacy of two anti-inflammatory medications (fenspiride and inhaled beclomethasone [beclomethasone dipropionate]) in patients with stable chronic obstructive pulmonary disease (COPD) over 6 months.

Design, methods and patients: This was a randomised comparison of 58 patients with COPD, divided into five treatment groups: fenspiride (stages 1 and 2), beclomethasone (stage 2), and two control groups (stages 1 and 2). In addition, 64 patients with exacerbations of COPD were evaluated over a 2-week treatment period during which they received either fenspiride or prednisolone. Clinical signs and symptoms of COPD were evaluated every 2 months (aggregated numerical index of signs and symptoms), as were lung function tests (forced vital capacity [FVC], forced expiratory volume in 1 second [FEV_1], FEV_1/FVC) and a 6-minute walking test.

Results: Statistically significant reductions in all evaluated COPD signs and symptoms were achieved with fenspiride in stage 1 COPD. Fenspiride therapy significantly reduced the indices of sputum parameters (8-fold decrease), incidence of dry rales (6-fold decrease), dyspnoea (4-fold decrease) and cough (2.5-fold decrease). In comparison with beclomethasone, fenspiride was superior in stage 2 COPD. In patients with stage 2 COPD, reductions were less marked, but remained significantly superior in the fenspiride group in comparison with the beclomethasone group and the control groups. In patients with exacerbations of COPD, fenspiride had equivalent efficacy to that of systemic corticosteroids.

Conclusion: Anti-inflammatory therapy with fenspiride in addition to bronchodilators significantly improved clinical signs and symptoms, external respiratory function tests and physical activity tests in patients with stage 1 COPD. Adjunc-

tive fenspiride therapy was superior to inhaled beclomethasone in stage 2 COPD. Anti-inflammatory therapy in COPD may be more effective at an early stage of this disease.

Chronic obstructive pulmonary disease (COPD) is a major global health problem that the WHO predicts will become the third most common cause of death by the year 2020.[1,2] COPD is the only major disease with increasing mortality in the world at present.[2]

COPD is a disease characterised by progressive airflow obstruction of the peripheral airways. It is associated primarily with lung inflammation as well as emphysema and mucus hypersecretion.[1] COPD has been defined in relation to the degree of airflow limitation,[3] and is not only a disease of the lungs but also a systemic inflammatory disorder.[3] In stable COPD it has not been shown how this systemic inflammation develops, but it is clear that the intensity of the systemic inflammation is directly linked to the severity of airflow obstruction.[4] However, recent experimental evidence has shown that regulation of the systemic inflammatory component does not necessarily correlate with control of the pulmonary inflammation.[5]

Bronchodilators form the cornerstone of pharmacological treatment for COPD, but they have not been shown to influence the decline in forced expiratory volume in 1 second (FEV_1) over time, as they do not alter the underlying inflammatory process in COPD.[6] Furthermore, bronchodilators do not improve survival in patients with COPD. Recently, long-acting β_2-adrenoceptor agonists have been shown to improve symptom management in patients with COPD, and currently the focus is on anti-inflammatory medications to prevent decline in FEV_1 and deterioration in lung function in patients with COPD.[6,7]

Fenspiride is an anti-inflammatory agent with promising initial results in patients with COPD.[1,8,9] It was therefore decided to undertake this study to examine the clinical effectiveness of fenspiride at two stages of COPD (stages 1 and 2) and in comparison with inhaled beclomethasone (beclomethasone dipropionate) in stage 2 COPD.

Materials and Methods

Patient Selection

One hundred and twenty-two patients with COPD were selected, of whom 79 were male and 43 were female; their median age was 57 ± 11 years. Eighty patients were smokers (60 male, 20 female), and the average smoking index was 224 ± 10 packets per year, with an average pack-year index of 30. Inclusion criteria were clinically diagnosed COPD. Exclusion criteria were patients on active therapy.

The patients were randomly divided into two groups: the study group (73 patients) and the control group (49 patients).

All patients received bronchodilator therapy with ipratropium bromide and β_2-adrenoceptor agonists (ipratropium bromide/fenoterol hydrobromide [Berodual®, Boehringer Ingelheim, Vienna, Austria])[1], in doses related to the degree of bronchial obstruction. After 3 weeks of bronchodilator therapy, changes in FEV_1 allowed determination of the stage of COPD to be confirmed.

Ethical approval was obtained from the Ethics Committee of the Central Research Institute, Moscow, Russia. The participants provided informed consent.

1 The use of trade names is for product identification purposes only and does not imply endorsement.

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Treatment of Patients with Stable Stage 1 and 2 Chronic Obstructive Pulmonary Disease (COPD)

Thirty-five patients in the study group had stable stage 1 and 2 COPD. These patients were divided into the following three treatment groups:

- Group F1: 12 patients with stage 1 COPD who were administered fenspiride at a dose of 80mg twice daily for 6 months.
- Group F2: 13 patients with stage 2 COPD who were administered fenspiride at a dose of 80mg twice daily for 6 months.
- Group B2: 10 patients with stage 2 COPD who were given beclomethasone inhalation at a dose of 200mg twice daily for 6 months.

In the control group (bronchodilator therapy only), ten patients with COPD stages 1 and 2 and 13 patients with COPD stage 2 were followed up for the 6-month period.

Examination of all COPD patients was carried out prior to commencement of therapy, 1 month after initiation of therapy, then at 2-monthly intervals for the total 6 months' study duration.

Treatment of Patients with Exacerbations of COPD

Sixty-four patients had non-infectious exacerbations of COPD. Twenty-six received bronchodilator therapy only (control group), 25 received fenspiride (80mg twice daily) for 2 weeks, and 13 received systemic corticosteroids (prednisolone 20mg daily for 1 week, then reduced gradually over the second week). In those patients with worsening COPD, inhaled beclomethasone was changed to oral prednisolone; when symptoms improved, beclomethasone was again introduced. Examinations were carried out prior to treatment, 1 week after initiation of therapy, and at the end of the second week.

Signs and Symptoms Evaluation Criteria

Clinical signs and symptoms of COPD were assessed individually, as were pulmonary function tests, i.e. forced vital capacity (FVC), FEV_1, FEV_1/FVC (modified Tiffeneau Index) and physical activity tolerance (6-minute walking test). In addition, clinical signs and symptoms of COPD were aggregated by means of a numerical scale and calculation of a cumulative index for each patient. This was derived as follows:

- Dyspnoea: 0 = absence of symptoms; 1 = minimum symptoms, not limiting activity; 2 = marked symptoms, limiting activity; 3 = significant limitation of activity.
- Cough: 0 = no symptoms; 1 = morning only; 2 = several (two to three) episodes per day; 3 = frequent (more than three) episodes per day.
- Rales: 0 = none; 1 = one temporary sound; 2 = one persistent sound; 3 = numerous persistent sounds.
- Sputum: 0 = none; 1 = small amount, disappearing; 2 = small amount, persisting; 3 = moderate amount, up to 50mL per day; 4 = >50mL per day.
- Night asphyxia: 0 = absent; 1 = occasional; 2 = once a week; 3 = daily.

Statistical Analyses

Statistical analyses were performed using standard international parametric and non-parametric methods. Chi-squared (χ^2) analyses were performed for all patients.

Results

COPD Patients

The five respiratory signs and symptoms listed above were evaluated over the 6-month observation period. Fenspiride therapy was particularly effective against respiratory signs and symptoms in stage 1 and 2 COPD (table I). The most significant reduction in respiratory symptoms with fenspiride related to sputum parameters, which showed a decrease in mean ± SD values from 2.58 ± 0.27 to 0.33 ± 0.18 ($p < 0.001$). The number of dry rales score decreased

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from 2.08 ± 0.18 to 0.33 ± 0.18 ($p < 0.001$). Dyspnoea score was reduced from 1.67 ± 0.18 to 0.46 ± 0.18 ($p < 0.001$). Cough score was reduced from 2.42 ± 0.18 to 0.63 ± 0.09 ($p < 0.001$). A similar tendency was noted in the group with stage 2 COPD treated with fenspiride, although improvements were substantially less than in stage 1 COPD patients. In comparison, the stage 2 COPD patients treated with beclomethasone demonstrated smaller reductions than those treated with fenspiride, particularly in relation to the following parameters: cough – from 2.30 ± 0.10 to 2.00 ± 0.21; sputum – from 2.20 ± 0.10 to 2.0 ± 0.21; and dry rales – from 1.90 ± 0.31 to 1.50 ± 0.31. Dyspnoea was reduced from 2.30 ± 0.21 to 2.10 ± 0.21. There was no regression of clinical signs and symptoms in the stage 2 COPD patients treated with beclomethasone in comparison with the control group.

Our clinical observations revealed significant changes in respiratory symptoms only in the groups treated with fenspiride. In stage 1 COPD patients they were noted by the first to second month of the study, reaching the maximum by the fourth month. Symptom regression in stage 2 COPD patients developed gradually by the sixth month.

Dyspnoea, an important symptom of COPD, decreased significantly by the second month of treatment in stage 1 COPD patients receiving fenspiride (from 1.67 ± 0.18 to 0.83 ± 0.18; $p < 0.001$) and continued to decrease up to the fourth month. There was less regression of dyspnoea in the beclomethasone-treated group, and the difference between the two groups was statistically significant by the fourth month (0.50 ± 0.09 and 1.30 ± 0.31; $p < 0.05$). In patients with COPD stage 2, dyspnoea decreased significantly during the first month of treatment with fenspiride and then remained at this level. There were no significant changes in dyspnoea in patients receiving beclomethasone and

Table I. Changes in the expression of respiratory signs and symptoms in patients with chronic obstructive pulmonary disease (COPD) after 6 months of therapy versus baseline. Values shown are points scored (mean ± SD) on a numerical scale for each sign or symptom

Symptom	Study group			Control group	
	COPD stage 1 (n = 12) [F1]	COPD stage 2 (n = 13) [F2]	COPD stage 2 (n = 10) [B2]	COPD stage 1 (n = 10)	COPD stage 2 (n = 13)
Dyspnoea					
prior to treatment	1.67 ± 0.18	2.0 ± 0.17	2.30 ± 0.21	1.70 ± 0.21	2.15 ± 0.17
after treatment	0.46 ± 0.18*	1.15 ± 0.17*	2.10 ± 0.21	1.20 ± 0.21	1.85 ± 0.17
Cough					
prior to treatment	2.42 ± 0.18	2.31 ± 0.17	2.30 ± 0.10	2.30 ± 0.10	2.23 ± 0.17
after treatment	0.63 ± 0.09*	0.92 ± 0.17*	2.00 ± 0.21	0.80 ± 0.31	1.85 ± 0.25
Rales					
prior to treatment	2.08 ± 0.18	1.77 ± 0.25	1.90 ± 0.31	2.00 ± 0.31	1.85 ± 0.25
after treatment	0.33 ± 0.18*	0.62 ± 0.17*	1.50 ± 0.31	1.60 ± 0.31	1.54 ± 0.25
Sputum					
prior to treatment	2.58 ± 0.27	2.31 ± 0.17	2.20 ± 0.10	2.40 ± 0.31	2.08 ± 0.33
after treatment	0.33 ± 0.18*	0.85 ± 0.25*	2.00 ± 0.21	1.90 ± 0.10	1.85 ± 0.33
Night symptoms					
prior to treatment	1.0 ± 0.27	0.35 ± 0.21	0.20 ± 0.10	0.30 ± 0.21	0.23 ± 0.8
after treatment	0*	0	0	0.10 ± 0.10	0.15 ± 0.08
Cumulative index					
prior to treatment	1.95 ± 0.14	1.75 ± 0.18	1.78 ± 0.14	1.74 ± 0.14	0.71 ± 0.15
after treatment	0.35 ± 0.11*	0.71 ± 0.13*	1.52 ± 0.10	1.32 ± 0.10	0.45 ± 0.05

B = beclomethasone; **F** = fenspiride. * $p < 0.05$, significantly different from baseline.

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Table II. Changes in pulmonary function tests (PFTs) in patients with stage 1 and stage 2 chronic obstructive pulmonary disease (COPD) after 6 months of therapy versus baseline. Values shown are mean ± SD for parameter

PFT parameter (%)	Study group						Control group			
	COPD stage 1(n = 12) [F1]		COPD stage 2 (n = 13) [F2]		COPD stage 2 (n = 10) [B2]		COPD stage 1 (n = 10)		COPD stage 2 (n = 13)	
	prior to treatment	after treatment	prior to treatment	after treatment	prior to treatment	after treatment	prior to treatment	after treatment	prior to treatment	after treatment
FVC	80.75 ± 4.22	92.81 ± 2.63*	73.49 ± 4.09	81.62 ± 4.09	74.42 ± 3.36	72.77 ± 2.18	85.31 ± 4.16	89.75 ± 3.26	75.75 ± 1.66	76.26 ± 2.06
FEV_1	69.81 ± 3.82	83.00 ± 2.89**	51.62 ± 3.11	57.29 ± 2.77	55.51 ± 2.55	50.89 ± 1.84	76.57 ± 2.48	75.52 ± 1.66	55.48 ± 2.22	54.03 ± 1.96
FEV_1/ FVC ratio	86.81 ± 2.52	89.38 ± 1.33	71.17 ± 3.77	70.75 ± 3.24	75.26 ± 2.84	70.21 ± 2.78	91.36 ± 3.65	85.36 ± 4.93	72.90 ± 1.59	68.64 ± 1.19

B = beclomethasone; **F** = fenspiride; **FEV_1** = forced expiratory volume in 1 second; **FVC** = forced vital capacity; * $p < 0.05$ vs baseline; ** $p < 0.001$ vs baseline.

in the control group during the 6 months of observation.

The changes in cough intensity that occurred with different treatment regimens for COPD demonstrated a significant effect of fenspiride on this respiratory symptom. Neither beclomethasone nor bronchodilator monotherapy had any significant effect on the severity of cough.

The change in auscultative signs was similar to the change in cough intensity; only fenspiride had a significant effect on this parameter. The decrease in rales was seen during the first month of treatment for stage 1 COPD patients and by the second month in stage 2 COPD patients, and then remained stable until the end of the study. Beclomethasone and bronchodilators did not have a significant effect on auscultative symptoms.

The effects of treatment on sputum parameters in different patient groups were similar to those on cough and rales parameters in COPD patients. Symptom regression was significant in patients undergoing treatment with fenspiride. A greater and more rapid symptom regression was registered in stage 1 COPD patients compared with stage 2 pa-

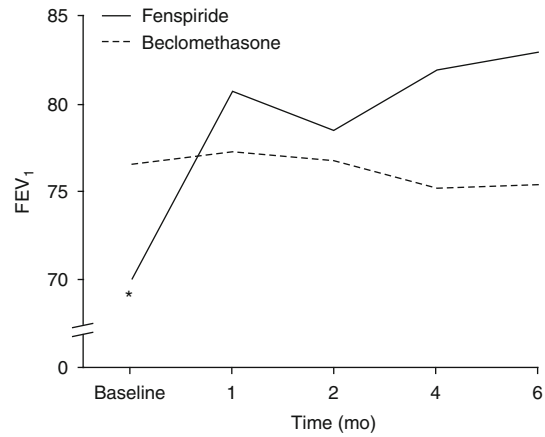

Fig. 1. Forced expiratory volume in 1 second (FEV_1) of patients with stage 1 chronic obstructive pulmonary disease during 6 months of therapy with either fenspiride or beclomethasone. * $p < 0.001$.

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Table III. Changes in physical activity tolerance (6-minute walking test) in patients with stage 1 and stage 2 chronic obstructive pulmonary disease (COPD) after 6 months of therapy versus baseline. Values shown are mean ± SD

Group	Prior to treatment (m)	At 2 months of treatment (m)	Increase on baseline at the 2nd month (%)	At 4 months of treatment (m)	Increase on baseline at the 4th month (%)	At 6 months of treatment (m)	Increase on baseline at the 6th month (%)
COPD stage 1 (n = 12) [F1]	403.83 ± 18.60	447.17 ± 15.06	10.73	461.25 ± 14.7*	14.22	473.58 ± 15.94	17.27
COPD stage 1 (n = 10) [control]	412.50 ± 18.48	414.2 ± 16.22	0.41	417.00 ± 13.35	1.09	421.03 ± 16.43	2.13
COPD stage 2 (n = 13) [F2]	351.70 ± 26.69	385.10 ± 23.61	9.50	396.70 ± 25.67	12.79	401.60 ± 26.69	14.9
COPD stage 2 (n = 10) [B2]	345.50 ± 19.51	363.50 ± 18.99	5.21	369.50 ± 18.48	6.95	368.50 ± 18.48	6.66
COPD stage 2 (n = 13) [control]	389.23 ± 15.8	390.77 ± 15.78	0.40	396. 15 ± 14.95	1.78	400.77 ± 15.78	2.96

B = beclomethasone; **F** = fenspiride; * $p < 0.05$ vs control.

tients. There were no reliable changes in sputum parameters in other patient groups.

Table II sets out the results of pulmonary function tests (FVC, FEV_1) during the 6-month treatment period. The results showed significant prolonged changes in pulmonary function test parameters only in stage 1 COPD patients treated with fenspiride. Specifically, FEV_1 normalised (from 69.81 ± 3.82L to 83.0 ± 2.89L; $p < 0.05$) and FVC increased (from 80.75 ± 4.22L to 92.81 ± 2.63L; $p < 0.05$) compared with baseline. The other patient groups showed no significant effect on external respiratory function parameters with treatment.

Figure 1 shows changes in FEV_1 parameters in COPD patients during the 6-month observation period. Only stage 1 COPD patients treated with fenspiride had an increase in FEV_1. A significant improvement in FEV_1 (from 69.81 ± 3.82L to 80.68 ± 2.91L; $p < 0.05$) was seen after 1 month's treatment with fenspiride; subsequently, this parameter remained relatively stable. There were no significant changes in FEV_1 in the other patient groups.

The results of a 6-minute walking test (table III) showed that only stage 1 COPD patients treated with fenspiride experienced significant improvement in this parameter. Furthermore, the significant increase in tolerance to physical activity was evident in this group by the fourth month of the study, both compared with baseline (walking distance increased by 14.22%: from 403.83 ± 18.60m to 461.25 ± 14.7m; $p < 0.05$) and with the control group (461.25 ± 14.7m vs 417.00 ± 13.35m, respectively; $p < 0.05$). The other patient groups experienced no significant increases in 6-minute walking distance by the end of the study. However, a tendency to increased walking distance was noted in COPD stage 2 patients treated with fenspiride. Measurement of the increased tolerance to physical activity in fenspiride groups showed that most improvement occurred in the second month of the study (in stage 1 COPD patients the increase in walking distance from baseline by

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Table IV. Exacerbations of chronic obstructive pulmonary disease (COPD) with anti-inflammatory treatment in patients receiving fenspiride (F) or beclomethasone (B) for 6 months

Parameter	Study group						Control group			
	COPD stage 1 (n = 12) [F1]		COPD stage 2 (n = 13) [F2]		COPD stage 2 (n = 10) [B2]		COPD stage 1 (n = 10)		COPD stage 2 (n = 13)	
	prior to treatment	after treatment	prior to treatment	after treatment	prior to treatment	after treatment	prior to treatment	after treatment	prior to treatment	after treatment
No. (± SD) of exacerbations per year	2.3 ± 0.27	0.5 ± 0.09*	2.3 ± 0.29	0.9 ± 0.17*	2.6 ± 0.31	1.0 ± 0.21*	2.2 ± 0.21	1.9 ± 0.21	2.1 ± 0.17	1.8 ± 0.08
Reducion factor (before/after) in number of exacerbations per year	4.66		2.4		2.65		1.18		1.16	

the second month was +10.73%, and in stage 2 COPD patients the increase was +9.50%); the additional increases in 6-minute walking distance seen at 4 and 6 months were smaller.

Table IV presents data on the effect of the different treatment regimens on the frequency of COPD exacerbations. All patients receiving anti-inflammatory therapy with fenspiride (stage 1 and 2 COPD) or beclomethasone (stage 2 COPD) had a statistically significant decrease in the frequency of exacerbations. There was no such decrease in the control group.

Table V presents changes in the main respiratory symptoms in COPD patients during exacerbation when no anti-inflammatory therapy is required. The data show that the effects of treatment with fenspiride and prednisolone on the expression of clinical signs and symptoms of COPD were similar.

Adverse Reactions

Overall tolerance of therapy was satisfactory. Adverse effects were observed in 13 COPD patients treated with fenspiride; these were minor adverse effects that required no additional therapy. Three asthenic women (with a low bodyweight) required a reduced dose of medication. Medication was discontinued for one patient only (because of an allergic reaction). Drowsiness and nausea resolved without intervention within 1 week after beginning treatment.

In the patient group receiving inhalation corticosteroids as basic COPD therapy, three of ten patients experienced mild adverse effects (two cases of dry cough, and one case of sore throat and dryness in the mouth). These adverse effects resolved without any intervention.

We also observed adverse effects, although rare, in the control groups (taking ipratropium bromide and Berodual® therapy) in four of 23 patients. Tachycardia and tremor were noted in two patients taking Berodual®, who consequently required re-

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Table V. Changes in respiratory signs and symptoms during exacerbations of chronic obstructive pulmonary disease (COPD) as a result of 2 weeks' anti-inflammatory therapy with either fenspiride (F) or prednisolone (P). Values shown are points scored (mean ± SD) on a numerical scale for each sign or symptom

Parameter	Study group						Control group			
	COPD stage 1 (n = 12) [F]		COPD stage 2 (n = 13) [F]		COPD stage 2 (n = 13) [P]		COPD stage 1 (n = 13)		COPD stage 2 (n = 13)	
	prior to treatment	after treatment	prior to treatment	after treatment	prior to treatment	after treatment	prior to treatment	after treatment	prior to treatment	after treatment
Dyspnoea	1.75 ± 0.14	0.69 ± 0.14*	2.42 ± 0.09	1.25 ± 0.18*	2.38 ± 0.08	1.35 ± 0.17*	1.77 ± 0.17	1.46 ± 0.25	2.46 ± 0.17	2.00 ± 0.17
Cough	2.13 ± 0.14	0.97 ± 0.14*	2.25 ± 0.27	1.46 ± 0.18**	2.38 ± 0.08	1.35 ± 0.17*	2.08 ± 0.17	1.77 ± 0.25	2.38 ± 0.17	1.96 ± 0.17
Rales	1.88 ± 0.21	0.88 ± 0.21*	1.92 ± 0.18	0.92 ± 0.18*	2.15 ± 0.17	1.15 ± 0.08*	1.92 ± 0.17	1.23 ± 0.25**	2.00 ± 0.17	1.62 ± 0.08
Sputum	2.13 ± 0.28	1.09 ± 0.21*	3.17 ± 0.18	1.71 ± 0.27*	2.92 ± 0.17	1.85 ± 0.17*	2.08 ± 0.25	1.85 ± 0.25	3.00 ± 0.17	2.62 ± 0.17
Night symptoms	0.75 ± 0.21	0.19 ± 0.14**	0.63 ± 0.27	0.25 ± 0.27	0.92 ± 0.25	0.08 ± 0.08**	0.38 ± 0.17	0.31 ± 0.17	0.54 ± 0.25	0.08 ± 0.08
Cumulative index	1.73 ± 0.08	0.68 ± 0.11*	2.08 ± 0.16	1.12 ± 0.16*	2.15 ± 0.08	1.15 ± 0.12*	1.65 ± 0.12	1.32 ± 0.2	2.08 ± 0.10	1.65 ± 0.07**

* $p < 0.05$ vs baseline, ** $p < 0.004$ vs baseline.

ductions in dosage. Concomitant adverse effects with ipratropium bromide (dry mouth and bitter taste) were noted in two subjects. No adverse effects required discontinuation of treatment.

Discussion

Current treatment for COPD has failed to halt the relentless progression of this disease.[10] At present, the best treatment for COPD is prevention through cessation of smoking.[2] Improved understanding of the pathogenesis of COPD has revealed new therapeutic targets that may impact on the future management of this disorder.[3] Inflammatory mediators are the focus of much current research.[10] In a review of future approaches to the treatment of COPD, Barnes and Stockley highlighted the need for treatments that suppress the inflammation in small airways and lung parenchyma.[6]

Anti-inflammatory agents have a potential future role as adjunctive therapy in COPD.[8] Promising results have been obtained with fenspiride.[8,11,12] Recent US guidelines reinforce the concept of tailoring COPD treatment in accordance with disease severity.[2]

In this study, fenspiride had a statistically significant effect on stage 1 COPD in comparison with controls. The most significant results of fenspiride therapy related to the reduction of sputum parameters (8-fold decrease in index), dry rales (6-fold decrease), dyspnoea (4-fold decrease) and cough (2.5-fold decrease). In stage 2 COPD, these decreases were less marked but still significant.

In comparison with patients treated with inhaled beclomethasone, fenspiride was superior in patients with stage 2 COPD. However, because of the small numbers in the treatment groups, statistical significance could not be said to be robust. Further studies with anti-inflammatory agents are necessary in patients with early-stage COPD, as these initial results point to an adjunctive effect for agents such as fenspiride.

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No significant differences were noted between fenspiride and corticosteroid therapy in the exacerbation phase of COPD.

More research is necessary to understand the cellular and molecular mechanisms of COPD, and to develop treatments that suppress the systemic and pulmonary inflammatory components of this disease.[6]

Conclusions

The results of this study demonstrated advantages of COPD treatment not only with bronchodilating agents, but also with adjuvant anti-inflammatory therapy with fenspiride. The study compared the clinical efficacy of two anti-inflammatory medications (inhaled beclomethasone and fenspiride) for treatment of stable COPD for 6 months. Adjunctive fenspiride treatment was shown to be beneficial overall, while beclomethasone reduced the number of exacerbations. These results show that the efficacy of anti-inflammatory therapy was related to stage of COPD. The efficacy of treatment with fenspiride was significantly greater during the first stage, and FEV_1 regression was effectively controlled by fenspiride at this early stage of COPD.

This study shows that anti-inflammatory therapy with fenspiride, in addition to bronchodilators, significantly improves clinical signs and symptoms, external respiratory function tests and physical activity tests in patients with stage 1 COPD. Adjunctive fenspiride therapy is superior to inhaled beclomethasone in stage 2 COPD. Anti-inflammatory therapy of COPD may be more effective in patients with stage 1 of the disease.

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