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Corticosteroid withdrawal in COPD

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Keywords

Chronic obstructive pulmonary disease, inhaled corticosteroids, pulmonary infection

Comments

The reason for so many patients suffering an exacerbation with a short period of stopping steroids may be due to rebound of suppressed lymphocytes and eosinophils. These data suggest that exacerbations occur frequently and relatively quickly on stopping inhaled steroids. Whilst this was only an observational study on the run in period to a different trial, there would seem to be a case for continuing inhaled steroids throughout a patient's stay in intensive or high dependency care.

Introduction

The effect of withdrawing inhaled corticosteroids on disease control in chronic obstructive pulmonary disease (COPD) is not known. This observational study reports the number of exacerbations of disease in patients recruited for the Inhaled Steroids in Obstructive Lung Disease (ISOLDE) trial. Inhaled corticosteroids improve FEV1, symptom control and bronchial reactivity in patients with bronchial asthma and the withdrawal of inhaled corticosteroids in both stable and unstable asthma produces relapse. Oral steroids produce significant improvements in FEV1 in about 20% of patients with COPD. Data on withdrawal of these drugs are not available. The ISOLDE trial is prospective and aims to recruit patients with COPD who can be shown to be stable off inhaled corticosteroids and hence the run in phase of this trial provided the opportunity to study patients who had had this treatment withdrawn.

Aims

To test the hypothesis that clinical exacerbations would occur more often in patients who had inhaled corticosteroids stopped in comparison to those not treated with the drugs.

Methods

Patients were recruited from six UK centres, aged 40-75 years and had a history of COPD. Patients with features or diagnosis of asthma were excluded. All patients had evidence of airflow obstruction and an FEV1 of less than 70% predicted after receiving inhaled salbutamol. All had been clinically stable for 3 months prior to the trial and those on oral prednisolone were excluded. Initial data collected consisted of smoking history, spirometry and assessment of reversibility and measurement of transfer factor for carbon monoxide and transfer co-efficient (DLCO and KCO).

Patients taking inhaled corticosteroids were told to stop at 6-8 weeks. An exacerbation was said to have occurred if there was 'an episode of increased shortness of breath requiring treatment with antibiotics with or without oral prednisolone'. The data were analysed with appropriate statistical tests.

Results

Of the 272 patients recruited, the majority (72%) were male. There were no differences in patient characteristics between the six participating centres. Fifty-nine percent of the patients were receiving inhaled corticosteroids when enrolled in the study, and there were no significant differences between this group and those not on inhaled steroids apart from the fact that those on inhaled steroids had a longer duration of symptoms. Twenty-five percent of the patients had at least one exacerbation within 8 weeks of enrollment, 82% of these occurred within 1 month. Ninety percent of those with an exacerbation had previously received oral steroids compared to 48% of those without (odds ratio 9.5 95% CI 4.0-23.3, $P < 0.001$). There was no correlation between total dose of inhaled steroids and time taken to relapse.

Discussion

There is increasing evidence that airway inflammation is a frequent finding in COPD and may respond to steroids. This is the first report to suggest that cessation of inhaled steroids may lead to a clinically significant deterioration. The value of this paper is somewhat limited by the observational nature but this is offset by the large number of patients studied. Potential errors may also have occurred due to the short period of follow up on which the conclusion is based. The relapse rate for COPD in other studies is 1.5 episodes per year thus a longer period of study is required before a chance finding can be excluded. No predictive marker could be found for the patients developing exacerbations suggesting that the initial clinical picture is a poor guide to whether the individual will improve on starting steroids or deteriorate on stopping them.

References

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