Long-term inhaled corticosteroid therapy in chronic airways obstruction

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Patients with chronic asthma and chronic obstructive pulmonary disease (COPD) may show continuous deterioration of lung function, possibly leading to disability or death. Patients with both chronic airflow obstruction and a past history of asthma have a smaller fall in forced expiratory volume in one second (FEV₁) when compared to obstructive patients without a past history of asthma [1]. However, in some patients with severe asthma, lung function may decrease between attacks and this may persist into early adulthood [2]. In some older asthmatic patients, a severe persistent impairment of lung function may be difficult to distinguish from that of non-asthmatic, smoking patients with COPD [1]. This observation presumes that, in these asthmatic patients lung function has declined excessively, as has been observed in some previous studies [3, 4]. In studies of COPD, the measured rate of decline of FEV₁ has varied from 48 to 91 ml·y⁻¹ and this appears to be related to the initial level of lung function [5] and to the degree of bronchial hyperresponsiveness to histamine [6]. High rates of decline in lung function may be found in smokers with mild preclinical COPD. Cessation of smoking is associated with a significant slowing down in the deterioration of lung function [3, 6].

There is little doubt that corticosteroids, particularly in the inhaled form, are effective treatments for asthma, causing effective symptom control and improvement in bronchial hyperresponsiveness, which may persist for up to one year [7-9]. Their role in COPD is less clear and remains controversial. In several studies [10-13], short-term treatment with oral corticosteroids has not resulted in overall improvement in COPD patients. However, in a retrospective study, the long-term use of more than 7.5 mg of prednisolone per day was associated with a slower decline in FEV₁ in patients with moderate to severe airflow obstruction [14, 15].

A few reports have been published on short-term treatment with inhaled steroids in COPD patients. Several studies have shown no significant effect of inhaled corticosteroids administered over a period of 8-12 weeks on FEV₁, or airway responsiveness to histamine [16-19]. In one study of inhaled corticosteroids given over 2 weeks, only 12 out of 34 COPD patients responded with a ≥10% increase in FEV₁, forced vital capacity (FVC) and peak expiratory flow rate (PEFR) but the group studied comprised patients with an allergic background [20].

The study of Dompebling et al. [21] published in this issue of the Journal is one of the first to examine the effect of inhaled steroid therapy, during a whole year, in patients with obstructive lung disease. The patients were categorized into an asthmatic group and a COPD group and were selected from a larger group originally entered for another study on the basis of a rapid yearly fall in FEV₁ [22]. The decline observed in both groups was unusually high (mean fall of ~160 ml·y⁻¹), particularly for the asthmatic group, when observed over a two year period, during which the effect of bronchodilator drugs was being investigated. During the third year, each group was treated with inhaled beclomethasone dipropionate (BDP, 800 μg·day⁻¹). BDP attenuated the rate of decline in FEV₁ in both asthma and COPD during the first 6 months but not during the last 6 months, with a greater effect in the asthma group. Not surprisingly, the provoking concentration producing a 20% fall in FEV₁ (PC₂₀) improved markedly in the asthmatics, but not in the COPD group. In both groups, the diurnal variation of PEFR and the symptom score improved.

The study of Dompebling et al. [21], can be criticized, particularly in relation to its design and selection of patients. Its study population is clearly unusual and highly selective, with excessive yearly declines in FEV₁. In the asthmatic group, a relatively large number of current smokers (14 out of 28) was included, and the overlap in several features, such as the bronchodilator response, peak flow variation and bronchial hyperresponsiveness between the two groups should have been avoided. It is quite likely that some of these patients would have fallen into an "asthmatic bronchitis" label. Perhaps the most important deficiency, for a study that spans 2-3 yrs, is the lack of control groups, which would have allowed more accurate interpretation of the data. On the basis of the current data, it can only be justified to compare the asthmatic group to the COPD group. It is not easy to explain why the yearly decline in FEV₁, reappeared during the second half year of treatment after an initial improvement, particularly in the asthmatic group. In addition, a marked increase in PC₂₀ was observed 6 months before BDP treatment in the COPD group.

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One could argue that it is not unethical to include a group of COPD patients on placebo treatment when the issue of the long-term effects of inhaled steroid therapy in COPD remains unclear. Undertaking such a study without encouraging patients to stop smoking before entry is probably more of an ethical issue, as is the withholding of inhaled steroid therapy from asthmatics with rapidly deteriorating airway function.

Despite these shortcomings, the study of Dompling et al. [21] indicates that among patients with an excessively rapid decline in FEV₁, the patients with COPD demonstrate smaller long-term improvements in FEV₁ and PEFR with inhaled BDP for up to one year than the patients with asthma. These results can only apply to those with rapid decline in FEV₁, and Dompling et al. [21] have identified one particular group of asthma and COPD patients in whom long-term inhaled steroid therapy may be of benefit. A controlled study of inhaled steroid therapy compared to placebo alone over a minimum period of two years in predominantly COPD patients alone, with or without features of asthma or bronchial hyperresponsiveness, is thus urgently needed.

The issue of inhaled steroid therapy in COPD is an important one to resolve. In the meantime, it is reasonable for the clinician to institute inhaled steroid therapy to COPD patients who demonstrate some degree of reversibility to bronchodilators, of eosinophilia or allergy, or who have some past history of asthma, or may have shown a response to a trial of oral prednisolone. The results of Dompling et al. [21] suggest that those with an excessively yearly decline in FEV₁, irrespective of the label of asthma or COPD, should also be treated.

Results of further clinical trials in this area are awaited eagerly, in particular the 3 year controlled, multicentre European study of inhaled corticosteroid in COPD, which has recently been initiated [23].

References