Inhaled corticosteroids reduce the progression of airflow limitation in chronic obstructive pulmonary disease: a meta-analysis

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CRD summary
This review assessed inhaled corticosteroids in patients with chronic obstructive pulmonary disease (COPD). The authors concluded that treatment with inhaled corticosteroids for at least two years slows the rate of decline in lung function in patients with COPD. The authors’ conclusions are likely to be reliable.

Authors’ objectives
To assess the effects of inhaled corticosteroids (ICS) on the progression of airflow limitation in patients with chronic obstructive pulmonary disease (COPD).

Searching
MEDLINE (from 1966 to February 2003), CINAHL (from 1982 to February 2003), International Pharmaceutical Abstracts (from 1970 to February 2003) and the Cochrane Controlled Trials Register (end of 2002) were searched. The reference lists in retrieved studies were also screened. Additional data and unpublished studies were sought through discussions with experts in the field who attended the 2002 American Thoracic Society international meeting. Studies reported only as abstracts were excluded.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion if they followed up patients for at least 1 year. All of the included studies followed up patients for at least 2 years (range: 24 to 40 months).

Specific interventions included in the review
Studies of ICS were eligible for inclusion. The included studies compared the following ICS with placebo: fluticasone, triamcinolone, beclomethasone and budesonide.

Participants included in the review
Studies of patients with stable COPD were eligible for inclusion, whereas patients with asthma were excluded. Where studies included mixed populations with asthma or COPD, data were only extracted for patients with COPD. In the included studies, the mean age ranged from 52.4 to 67.6 years, the mean forced expiratory volume in 1 second (FEV1) as a percentage of predicted ranged from 39.7 to 86.9%, the mean percentage of reversibility ranged from 2.8% to an estimated 11.5%, and the percentage of smokers ranged from 34 to 100%.

Outcomes assessed in the review
Studies that measured the change in FEV1 over time as the primary outcome were eligible for inclusion. The primary outcome in the review was the annual change in FEV1 decline rate.

How were decisions on the relevance of primary studies made?
All five authors independently screened the identified papers for inclusion and resolved any disagreements on study selection through discussion and consensus.

Assessment of study quality
The authors did not state that they assessed validity.
Data extraction
Data were extracted and confirmed by consensus. The authors did not state how many reviewers were involved. The extracted data included the number of patients per treatment group, the treatment and characteristics of the patients (e.g. age, lung function and smoking status).

For each treatment group within each study, the annual change in FEV1 and the difference in the annual change between treatment groups were calculated. In all but one study the mean annual change in FEV1 was modelled, taking account of the correlation between repeated measures. In one study that reported the median rather than the mean change in FEV1, it was assumed that the median approximated the mean and the standard error of the mean was estimated from the reported P-value (attempts to obtain the mean from the study authors were unsuccessful).

Methods of synthesis
How were the studies combined?
The studies were combined using a meta-analysis. The pooled rate of difference between treatments in the rate of decline in FEV1, together with the 95% confidence interval (CI), was calculated using the random-effects model of DerSimonian and Laird. The results for COPD patients from 3 studies were combined before pooling them with the other 5 original studies. The potential for publication bias was assessed using a funnel plot and the Egger test.

How were differences between studies investigated?
Forest plots were created and statistical heterogeneity was assessed using the Q statistic. Sensitivity analyses were performed to assess the effects of high-dose ICS and the effects in patients with a baseline FEV1 of 50% or less of that predicted.

Results of the review
Data from 8 individual RCTs (3,715 patients) were included. Three of these studies were reported in one secondary analysis paper.

ICS significantly reduced the rate of decline in FEV1 by 7.7 mL/year (95% CI: 1.3, 14.2, P=0.02), based on 5 plus 3 combined studies. No significant heterogeneity was detected (P=0.32).

There was a greater reduction in the rate of decline of FEV1 in studies using high-dose ICS (4 RCTs, 2,416 patients); the reduction was 9.9 mL/year (95% CI: 2.3, 17.5, P=0.01). No significant heterogeneity was detected (P=0.50).

There was a non significant trend towards a reduction in the rate of decline in patients with a baseline FEV1 of 50% or less of that predicted (1,032 patients); the reduction was 18.3 mL/year (95% CI: -1.5, 38.0, P=0.07), based on 2 plus 3 combined studies. No significant heterogeneity was detected (P=0.25).

The asymmetrical funnel plot and Eggar test (P=0.03) suggested the possibility of publication bias.

Authors' conclusions
Treatment with ICS for at least 2 years slows the rate of decline in lung function in patients with COPD. This effect was greater with high-dose ICS.

CRD commentary
The review question was clear in terms of the study design, participants, intervention and outcomes. Several relevant sources were searched, the search terms were stated, and attempts were made to locate unpublished data. It was unclear whether any language limitations had been applied. Methods were used to minimise bias in the study selection and data extraction processes. Only RCTs were included, but the quality of the included studies was not assessed. The data were combined in a meta-analysis and statistical heterogeneity was assessed. The authors discussed some of the limitations of the review and the clinical importance of the improvement in FEV1. The conclusions appear reliable, but some data had to be extrapolated from the primary studies.
Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further trials are required to inform clinicians of the role of ICS, and to determine the effect of the initial increase in FEV1 on the overall effect of ICS.

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Other publications of related interest
These additional published commentaries may also be of interest. Greenstone M. Review: inhaled corticosteroids slow the progression of airflow limitation in COPD. Evid Based Med 2004;9:75. Greenstone M. Review: Inhaled corticosteroids slow the progression of airflow limitation in COPD. ACP J Club 2004;140:57.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.