Long-term effects of inhaled corticosteroids on FEV1 in patients with chronic obstructive pulmonary disease: a meta analysis

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CRD summary
This review evaluated the long-term effects of inhaled corticosteroids in patients with chronic obstructive pulmonary disease (COPD). It found that inhaled corticosteroids did not modify the long-term decline in lung function associated with COPD. This was a well-conducted review and, provided the primary randomised controlled trials are of reasonable quality, the authors' conclusions regarding long-term outcomes with inhaled corticosteroids appear reliable.

Authors' objectives
To evaluate the long-term effects of inhaled corticosteroids on the rate of forced expiratory volume (FEV1) decline in patients with chronic obstructive pulmonary disease (COPD).

Searching
MEDLINE, EMBASE, CISCOM, AMED and the Cochrane Library were searched from 1966 to December 2002. The authors checked retrieved references and other reviews and consulted experts about further relevant studies. Both English and non-English language sources were searched.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials (RCTs) that were placebo-controlled and had a minimum follow-up of 24 months were eligible for inclusion. The duration of follow-up in the included studies ranged from 24 to 54 months.

Specific interventions included in the review
Placebo-controlled trials of inhaled corticosteroids were eligible for inclusion. The included studies were of budesonide (400 to 800 microg twice daily), beclomethasone (750 to 1,000 microg twice daily), triamcinolone (600 microg twice daily) and fluticasone (500 microg twice daily). In all studies the comparator drug was placebo. No study permitted the use of both oral and inhaled corticosteroids.

Participants included in the review
Studies of patients with COPD, but not asthma, were eligible for the review. In the included studies, the proportion of male participants ranged from 60.4 to 100%, the mean age ranged from 52.4 to 66.6 years, and the proportion of active smokers ranged from 39 to 100%. The inclusion criteria for FEV1 at entry to the primary studies varied; details were reported. Most of the included studies excluded patients with a bronchodilator response to inhaled corticosteroids.

Outcomes assessed in the review
Studies that reported the decline in FEV1 were eligible for inclusion. The results of other outcomes reported in the primary studies were not reported in the review.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Studies were considered to be high quality if they had adequate randomisation and allocation concealment methods, were double-blind and conducted intention-to-treat analyses. The authors did not state how the quality criteria were applied, or how many reviewers performed the quality assessment.
Data extraction
Two reviewers independently extracted the data according to predetermined criteria. The difference in the mean change in FEV1 between treatment groups and its 95% confidence interval (CI) was calculated.

Methods of synthesis
How were the studies combined?
The results of the individual studies were combined using a fixed-effect model; a weighted mean difference (WMD) and 95% CI were calculated. A random-effects model was also conducted but the results were not reported, other than to say they did not differ significantly from those for the fixed-effect model.

How were differences between studies investigated?
Statistical heterogeneity was tested using the Q-test statistic (P<0.10 for significance). Subgroup analyses were also conducted, based on whether the patients had high or low FEV1 at baseline and whether FEV1 was measured before or after bronchodilator use.

Results of the review
Six RCTs (n=3,571) were included. All were available as full publications.

The quality of the included studies was not reported, except to say that some data were missing because of patient withdrawals (it was unclear how serious a problem this was).

There was no statistical heterogeneity between the included studies.

The pooled estimate indicated that treatment with inhaled corticosteroids produced no statistically significant effect on decline in FEV1 over time: the WMD was -5.0 mL/year (6 RCTs; 95% CI: -11.2, +1.2).

When the analysis was stratified by baseline FEV1, the pooled estimates were WMD -11.0 (95% CI: -23.1, +1.0) for FEV1 less than 51% predicted (n=949) and WMD -2.9 (95% CI: -10.1, +4.3) for FEV1 greater than 51% predicted (n=2,722).

Treatment differences were also non significant when the analysis was stratified by whether FEV1 was assessed before or after bronchodilator use.

Authors' conclusions
Inhaled corticosteroids did not modify the long-term decline in lung function associated with COPD.

CRD commentary
This review used clearly defined inclusion criteria to address a very specific research question. The literature searches were broad and were not restricted by language or publication type. One study, available only as an abstract, was excluded because relevant data could not be accessed; this might have affected the results. The possibility of publication bias was also not tested. The review methods were not described in detail, although some effort was made to reduce review bias by duplicate, independent data extraction. It was unclear how the quality of the included trials was assessed and the results of this assessment were not incorporated into the synthesis. It would have increased confidence in the review's findings if it were clear that the studies were of a good quality. The combining of the primary study results in a fixed-effect meta-analysis was appropriate. Provided the primary studies are of reasonable quality, the authors' conclusions regarding the long-term outcomes with inhaled corticosteroids appear reliable.

Implications of the review for practice and research
Practice: The authors recommended that inhaled corticosteroids are used for symptomatic patients who have a bronchodilator response to inhaled corticosteroids, or who have frequent COPD exacerbations that require the use of
oral corticosteroids or antibiotics. These recommendations do not appear to have arisen from the findings of the present review.

Research: The authors stated that additional studies into the effects of inhaled corticosteroids on quality of life, systemic side-effects and dose-response relationships in corticosteroid responsive patients, and economic evaluations of inhaled corticosteroids, are required.

Bibliographic details

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http://www.annals.org/cgi/content/full/138/12/969

Other publications of related interest
This additional published commentary may also be of interest. Inhaled corticosteroids in chronic obstructive pulmonary disease [letters]. Ann Intern Med 2003;139:864-5.

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Record Status
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.