Dose response of inhaled corticosteroids on bronchial hyperresponsiveness: a meta-analysis
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CRD summary
This review assessed the relationship between inhaled corticosteroid dose and bronchial hyperresponsiveness in patients with asthma. The authors concluded that high doses conferred greater improvements than low doses. The conclusions appear to follow from the evidence presented but it is difficult to comment on their reliability because of methodological and reporting limitations in the review.

Authors' objectives
To determine whether a dose-response effect exists between inhaled corticosteroids and bronchial hyper-responsiveness (BHR) in asthmatic patients.

Searching
MEDLINE, databases on BIDS, and the Cochrane Library were searched up to May 2001; the search terms were listed in the review. The search was limited to studies which had at least an English abstract.

Study selection
Study designs of evaluations included in the review
The inclusion criteria specified randomised placebo-controlled trials (RCTs) with either a placebo arm or placebo run-in period.

Specific interventions included in the review
The inclusion criteria specified interventions in which the doubling dose/dilution protection with inhaled corticosteroid was compared with a placebo. Interventions in which airway bronchoprotection was evaluated with either direct (methacholine and histamine) or indirect stimuli (adenosine monophosphate) were included. In all trials, BHR was tested after a steady state of at least 2 weeks was reached. All doses, delivery devices and type of inhaled corticosteroid were permissible.

Participants included in the review
The inclusion criteria specified asthmatic patients with BHR.

Outcomes assessed in the review
The inclusion criterion was the estimated doubling dose/dilution shift.

How were decisions on the relevance of primary studies made?
Two authors independently selected papers for the review from the lists of titles and abstracts. All authors then read the full papers to decide whether the studies should be included or excluded. Any discrepancies were resolved by discussion.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Data were extracted on the steroid dose, doubling dose protection, with 95% confidence interval (CI) compared with
placebo, bronchial stimulant, number of patients in the study and dosing of inhaled corticosteroid. The doses of fluticasone and mometasone were doubled to achieve a microgram equivalent dose to beclomethasone and budesonide. For comparison purposes, the doses of the inhaled corticosteroid were categorised as low/medium (less than 1,000 microg) or high (at least 1,000 microg).

**Methods of synthesis**

How were the studies combined?
For low/medium- and high-dose categories, the weighted estimate of overall protection was calculated for all studies and plotted on a log scale of doubling dose/dilution shift versus inhaled corticosteroid dose.

How were differences between studies investigated?
The authors did not state a method for assessing any differences between the studies.

**Results of the review**

Twenty-five RCTs with 963 participants were included in the review. Four trials were subdivided as data were available for a different bronchial challenge stimulus or different dose of inhaled corticosteroid. There were 18 low/medium-dose comparisons and 12 high-dose comparisons.

Compared with placebo, the estimated doubling dose/dilution shift for low/medium- and high-dose categories were 1.25 (95% CI: 1.08, 1.42) and 2.16 (95% CI: 1.88, 2.44), respectively.

**Authors' conclusions**

High doses of inhaled corticosteroids conferred greater improvements in BHR than low doses.

**CRD commentary**

The review could have been of higher quality with regard to the reporting of the review process, the validity assessment, and the assessment of heterogeneity for the included studies. The research question was clear, as were the inclusion and exclusion criteria. The literature search was limited in that it did not search EMBASE nor report any additional searches of bibliographies or unpublished literature sources. The review process could have been clearer in reporting who performed the data extraction and whether the validity of the included studies was assessed. The meta-analyses appear to have been appropriate, but statistical and clinical heterogeneity was not reported. The conclusions appear to follow from the results presented.

**Implications of the review for practice and research**

The authors did not state any implications for practice or further research.

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Subject indexing assigned by NLM

**MeSH**

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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.