Low-dose methotrexate spares steroid usage in steroid-dependent asthmatic patients: a meta-analysis
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Authors' objectives
To determine if treatment with low-dose methotrexate spares oral steroids in adult, steroid-dependent, asthmatic patients.

Searching
MEDLINE (1966 to November 1996), CINAHL (1982 to October 1996), Current Contents - Clinical Medicine and Life Sciences (November 27, 1995 to November 18, 1996) were searched for relevant articles (search terms given). Reference lists of included studies were examined for possible additional studies.

Study selection
Study designs of evaluations included in the review
Placebo-controlled, double-blind trials were included.

Specific interventions included in the review
Methotrexate (usually 3 to 4 months, 15 mg/week).

Participants included in the review
Adult asthmatics dependent on long-term oral steroids (prednisone or prednisolone) were included.

Outcomes assessed in the review
The outcomes assessed were steroid dosage, FEV1, serious side-effects and alteration in serum aspartate aminotransferase level.

How were decisions on the relevance of primary studies made?
Titles and/or abstracts of identified studies, and full articles if necessary, were examined by the author.

Assessment of study quality
The author does not state that they assessed validity.

Data extraction
The data were extracted by the author of the review only.

Methods of synthesis
How were the studies combined?
The effect size in standard deviations (SD) of the daily dosage of prednisone or prednisolone during methotrexate therapy, relative to the daily dosage during the placebo arm of the study, was calculated. Studies were weighted to obtain a summary measure of effect size, and 95% confidence intervals (CIs) were calculated.

How were differences between studies investigated?
No statistical test for heterogeneity was presented.

Results of the review
Eleven double-blind, placebo-controlled trials (n=233) were included. Seven of the included studies were of a
crossover design (n=106).

Methotrexate treatment resulted in a decrease in prednisone or prednisolone usage by an average of 4.37 mg/day or 23% of initial dosage. The summary effect size was -0.53 SDs (95% CI: -0.29, -0.77; p<0.05). Subgroup analysis showed that patients treated with prolonged therapy (6 months) with methotrexate, those with low long-term usage of steroids (20 mg/day or less) and those whose study design incorporated a run-in period, tended to have the greatest steroid-sparing effects with methotrexate. None of the 11 studies reported a significant change in pulmonary function as determined by FEV1. No life-threatening side-effects were reported in any of the included studies, although liver function was affected by methotrexate treatment in some studies.

Authors’ conclusions
Low-dose methotrexate has a significant steroid-sparing effect in steroid-dependent asthmatic patients. The greatest effect was evident in patients in whom an effort was made to reduce baseline steroid dosage and in whom methotrexate was used for 24 weeks.

CRD commentary
Little information is provided on the assessment of relevance and validity of the primary studies, although the review does provide adequate detail of the studies included. The pooling of the studies was well documented and the results were thoroughly discussed. There is, however, a Cochrane review in this area which concludes ‘there appears to be no case for the routine use of methotrexate in patients on long term steroids’. The Cochrane review included 13 RCTs (compared with 11 here) and assessed the validity of the included trials. Many of the trials were found to have methodological flaws. Consultation of the Cochrane review is advised (see Other Publications of Related Interest).

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Other publications of related interest

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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.