A systematic review of the adjunctive use of systemic corticosteroids for pulmonary tuberculosis

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CRD summary
This review assessed adjunctive systemic corticosteroids in the treatment of pulmonary tuberculosis (PTB). The authors concluded that adjunctive systemic corticosteroids can safely provide significant clinical and radiologic benefits for selected patients with advanced PTB. Since most of the included studies were conducted over 20 years ago, the relevance of the results to current practice is unknown.

Authors' objectives
To assess the safety and benefits of adjunctive systemic corticosteroids in the treatment of pulmonary tuberculosis (PTB).

Searching
MEDLINE, Index Medicus and Current Contents were searched to 2001 for studies published in English; the keywords were provided. Bibliographies of articles and major textbooks of pulmonary disease were also searched.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion if they presented adequate and complete statistical information (no details were reported).

Specific interventions included in the review
Studies of adjunctive systemic corticosteroids were eligible for inclusion. The studies had to report sufficient information on the treatment regimens. Studies that solely used corticosteroids for the management of pleural TB were excluded, as were studies only using intralobular or endobronchial administration of corticosteroids. The included studies used prednisone, prednisolone and/or adrenocorticotrophin (ACTH) as adjunctive treatment to multi-drug combination anti-TB regimens. These regimens included combinations of two or more of the following drugs: isoniazid, para-aminosalicylic acid, streptomycin, pyrazinamide, rifampin and ethambutol. The main daily dose of prednisone or prednisolone was 31 mg (range: 16 to 60) and the mean ACTH dose was 40 units. Corticosteroids were given for a mean of 85 days (range: 30 to 180). The included studies administered treatment in in-patient and/or out-patient settings.

Participants included in the review
Studies in patients with PTB were eligible for inclusion if the patients were diagnosed by acid-fast or fluorochrome smear, or sputum culture. Most of the patients in the included studies had moderate to severe disease and cavitation.

Outcomes assessed in the review
Studies that reported sufficient details of clinical, bacteriological and roentgenographic outcomes were eligible for inclusion. The review defined clinical response as an improvement in at least one of the following: time to defervescence; weight gain; time to normalisation of serum albumin and/or erythrocyte sedimentation rate (ESR); and length of hospital stay. The review defined radiographic response as a moderate or greater improvement in the clearing of parenchymal infiltrates and in the time until closure of cavities.

In all of the included studies, at least two blinded radiologists independently read the radiographs; the radiologic outcomes were assessed after 2 weeks to 12 months. The included studies generally defined bacteriologic response as either a decrease in sputum bacillary count or conversion of sputum smear (using acid-fast stain or fluorescent microscopy), or a change in culture from positive to negative.
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
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. The extracted data included the number of patients receiving systemic corticosteroids, the extent of radiological disease, corticosteroid and anti-TB treatment regimens, and results (classified as no significant difference or significant difference compared with control). For all of the included studies, a P-value of less than 0.05 was considered statistically significant.

Methods of synthesis
How were the studies combined?
Some characteristics of the included studies were summarised in the text of the review. The number of studies reporting a statistically significant difference between treatments was presented for each type of outcome measure.

How were differences between studies investigated?
Differences between the studies were not discussed.

Results of the review
Eleven RCTs (1,814 patients) were included.

Clinical outcomes (9 studies): all 9 studies showed that adjunctive corticosteroids significantly improved at least one outcome measure compared with no corticosteroid treatment. Measures for which improvement was significant included time to defervescence, weight gain (improved faster and to greater extent in 6 of 8 RCTs), normalisation of ESR (more rapid in 3 RCTs), normalisation of serum albumin (more rapid in 1 RCT) and hospital stay (reduced in 2 of 3 RCTs).

Radiographic outcomes (11 RCTs): 9 RCTs showed significantly greater and earlier improvement in clearing of parenchymal infiltrates with corticosteroids compared with control. Six RCTs showed a faster reduction in size and closure of cavities with corticosteroids.

Bacteriologic outcomes (11 RCTs): 7 RCTs showed no statistically significant difference between corticosteroids and no corticosteroids for the rate or speed of sputum conversion, while one found that corticosteroids slowed the time until sputum conversion and three found that corticosteroids reduced the time until conversion.

Authors’ conclusions
Adjunctive systemic corticosteroids can safely provide significant clinical and radiologic benefits for selected patients with advanced PTB.

CRD commentary
The review question was described in terms of the study design, intervention, participants and outcomes, but the reviewers did not specifically describe the level of information considered ‘sufficient’ for treatment regimes and statistical details. Several relevant sources were searched and the search terms were stated. No attempts were made to minimise language or publication bias. The methods used to select the studies and extract the data were not described, thus it is not known whether efforts were made to reduce errors and bias. Even though only RCTs were included, the quality of the included studies was not systematically assessed.
Only minimal information on the included studies was presented; in particular, there was little information on the characteristics of the patients and drop-outs were not reported. The reviewers only discussed the number of studies reporting positive results for the specified outcomes. Differences between the studies were not discussed. The reviewers discussed some of the limitations of the review, such as the lack of studies using more modern anti-TB treatment regimens. The majority of the studies were conducted in the 1960s to 1980s, so the relevance of the results to current practice is unknown. Given the limitations highlighted, the authors’ conclusions may be overstated.

**Implications of the review for practice and research**
The authors did not state any implications for practice or further research.

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