The effectiveness of glucocorticoids in treating croup: meta-analysis

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Authors' objectives
To assess the effectiveness of glucocorticoid treatment in children with croup.

Searching
The authors searched MEDLINE (January 1966 to August 1997) exploding glucocorticoid treatment (and each of the terms for corticosteroids) and croup. The authors also searched Excerpta Medica and EMBASE from January 1974 to August 1997 and the Controlled Trials Register of the Cochrane Library. Letters were also sent to the authors of trials published in the previous 5 years to request data from additional relevant published or unpublished trials.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) which used a previously validated strategy.

Specific interventions included in the review
Glucocorticoids (dexamethasone, budesonide and methylprednisolone) and placebo.

Participants included in the review
Children (n = 1,736) being treated for croup on an inpatient (14 trials) or outpatient (10 trials) basis. Children's ages ranged from 13 months to 45 months; the minimum age for inclusion was 4 months and the maximum age was 12 years.

Outcomes assessed in the review
Severity of croup, use of co-interventions, length of stay in accident and emergency or hospital, and rate of hospitalisation.

How were decisions on the relevance of primary studies made?
Two of the authors selected studies based on a review of the titles and abstracts. The complete text of these studies was then retrieved. All studies that were retrieved were then reviewed by two of the authors independently as to whether they met the review's inclusion criteria. The weighted Kappa score was used to measure integrate agreement.

Assessment of study quality
The authors used the Jadad 5-point scale to assess randomisation (0-2 points), double-blinding (0-2 points), and withdrawals and drop-outs (0-1 point). For component assessment, concealment of allocation was described either as adequate, inadequate, or unclear. Sponsorship of studies was also noted. Studies were assessed for quality by two of the authors independently and integrate agreement was measured by the interclass correlation. Differences were resolved by consensus.

Data extraction
Data were extracted by one reviewer and checked by a second reviewer from studies which had been masked to obscure the authors’ names and institutions, the location of the study, reference lists, and any other potential identifiers.

Data were extracted using a structured form that captured patient status (inpatient or outpatient), the intervention and its control, the name of the drug, the route of administration, and the dose. Additionally, data were collected on the primary outcome measure, clinical croup score at baseline and at any subsequent assessment times, length of stay in hospital or accident and emergency in hours, whether the patient had improved (yes or no), and the use of additional interventions such as adrenaline, supplemental glucocorticoids, mist treatment, incubation, or antibiotic treatment.
trial effect size (ES) was defined as the difference between the two treatments in the mean change from croup score at baseline. The authors derived effect sizes from cross sectional summaries for trials not reporting effect sizes directly.

**Methods of synthesis**

How were the studies combined?

A pooled standardised effect size was calculated for the trials with 95% confidence intervals (cis) using a fixed-effect model.

The standardised effect size was used to combine trials reporting different versions of the croup score. The quality score of the included trials was incorporated into the pooled estimates using the method proposed by Mother (see Other Publications of Related Interest).

How were differences between studies investigated?

Heterogeneity between studies was investigated using sensitivity and subgroup analyses performed on the primary outcome of the change in croup scores from baseline at 6 hours. The authors also assessed the effect of the concealment of treatment allocation on the pooled estimates.

**Results of the review**

Twenty-four RCTs with 1,736 participants met the inclusion criteria with a median of 40 participants in each trial. Five trials compared active treatments and 19 were placebo controlled. Dexamethasone was evaluated in 17 trials, bedizened in 9 trials and methyl prednisone in 3 trials. Some studies examined more than one drug.

Glucocorticoid treatment was associated with an improvement in the croup severity score at 6 hours with an ES of -1.0 (95% CI: -1.5, -0.6) and at 12 hours of -1.0 (95% CI: -1.6, -0.4). At 24 hours the improvement was no longer statistically significant (ES = -1.0, 95% CI: -2.0, 0.1).

The improvement in Wesley croup score subgroup at 6 hours was 2.8 (95% CI: 2.2, 3.5) for dexamethasone or bedizened versus 1.0 (95% CI: 0.3, 1.7) for placebo.

The number needed to treat (NOT) at 6 hours was 7, at 12 hours was 5, and at 24 hours was 8, patients needed to treat for one patient to experience improvement.

There was a decrease in the number of adrenaline treatments needed in children treated with glucocorticoids: a decrease of 9% (95% CI: 2%, 16%) among those treated with bedizened and of 12% (95% CI: 4%, 20%) among those treated with dexamethasone.

There was also a decrease in the length of time spent in hospital of a weighted mean difference of -11 hours (95% CI: -18, 4 hours), and inpatients hospital stay was reduced by 16 hours (95% CI: -31, 1 hour).

The interclass correlation between two reviewers was 0.63 for the Jadad score, 0.98 for allocation concealment, and 1.0 for sponsorship, indicating at least substantial agreement in all cases. The mean Jadad score was 3 (or 60%) for the best quality of reporting.

Publication bias did seem to play a part in these results. The trim and fill method suggested that seven small trials were suppressed because their results were not significant.

**Authors’ conclusions**

Dexamethasone and bedizened are effective in relieving the symptoms of croup as early as 6 hours after treatment. Fewer co-interventions are used and the length of time spent in hospitals is decreased in patients treated with glucocorticoids.

**CRD commentary**
This is a very good systematic review. The authors have clearly stated their research question and some inclusion and exclusion criteria. The literature search is good and the authors have not restricted the search to English language trials. The authors have also tested and adjusted for publication bias.

The quality of the included studies was formally assessed and the authors have reported in detail on how the articles were selected, and how many of the reviewers were involved in the data selection and extraction.

The data extraction is reported in tables and text and the statistical pooling was appropriate. There were tests for heterogeneity and the authors have discussed several methodological and data limitations in the review. The authors conclusions appear to follow from their results.

Implications of the review for practice and research
Practice: The authors state that, in the absence of further evidence, an oral dose of dexamethasone (probably 0.6 mg/kg) should be preferred because of its safety and efficacy. In a child who is vomiting, nebulose bedizened or intramuscular dexamethasone may be preferable.

Research: The authors state that further research may be warranted to investigate whether 0.15 mg/kg of dexamethasone is as effective as 0.6 mg/kg.

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Other publications of related interest


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