Effectiveness of corticosteroid treatment in acute pharyngitis: a systematic review of the literature

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CRD summary
This review concluded that, despite significant variation between included trials, there was some evidence that corticosteroid treatment for acute pharyngitis was associated with a relatively small reduction in time to clinically meaningful pain relief and pain relief at 24 hours. Overall, the authors acknowledged the limitations of the data and analyses, but their conclusions should be interpreted with appropriate caution.

Authors' objectives
To assess the effectiveness and tolerability of corticosteroids for pain relief of acute pharyngitis potentially caused by group A beta-haemolytic Streptococcus (GABHS) in adult and paediatric patients.

Searching
MEDLINE, EMBASE, the Cochrane Library, Scopus and BIOSIS Previews were searched for studies in any language up to June 2009. Search terms were reported. A citation search using the Web of Science was performed. Abstracts from three conferences (2005 to 2008) were hand-searched. Ongoing trials were identified through searching controlled trial registration websites. Topic experts were contacted. Reference lists of retrieved studies were screened for further data.

Study selection
Randomised controlled trials (RCTs) of corticosteroids for pain relief in adults and/or children with acute pharyngitis were eligible for inclusion in the review. The primary outcome was the reduction of pain measured both on a visual analogue scale (VAS) and as the time to clinically meaningful pain relief. The secondary outcome was the occurrence of adverse events.

Most of the included trials assessed the corticosteroid dexamethasone (5 to 10mg); other corticosteroids were betamethasone, prednisone, and cortisone. The dose, method of administration and treatment duration varied between trials (details reported in the review). Most of the included trials also used concomitant antibiotics.

The age of participants ranged from four to 65 years. Patients were mainly recruited from emergency departments (either urban or urban paediatric settings); one trial recruited patients from a family practice and another from a military hospital. Most trials were conducted in North America (mainly the USA); others were conducted in Korea, Israel and Turkey. Only four of the trials used a group A beta-haemolytic Streptococcus stratified analysis.

Two reviewers independently assessed the studies for inclusion; disagreements were resolved through consensus.

Assessment of study quality
The methodological quality of the trials was assessed by two reviewers using the criteria of the Cochrane Collaboration and the Jadad tool. The assessed criteria were adequacy of randomisation, allocation concealment, blinding, completeness of follow-up, presence of selective reporting, and presence of other biases. Each trial was awarded a Jadad score between 0 and 5 points.

Data extraction
Means and standard deviations (SDs) were extracted for continuous outcomes. Where trials reported means without standard deviation, they were calculated using other data, where possible. Authors were also contacted for missing data if necessary.

The authors did not state how many reviewers performed the data extraction.
Methods of synthesis
Trials were grouped by outcome and pooled weighted mean differences (WMDs), with 95% confidence intervals (CIs), were calculated using a random-effects model. Statistical heterogeneity was assessed using the $I^2$ statistic; values of 25, 50, and 75% were judged to represent low, moderate, and high degrees of heterogeneity.

Subgroup analyses were conducted to compare group A beta-haemolytic Streptococcus culture-positive and culture-negative patients; a planned subgroup analysis to compared adult versus paediatric patients was not possible.

Sensitivity analyses were also performed to compare random-effects versus fixed-effect models, and differences in methodological quality.

Results of the review
Ten RCTs were included in the review (n=1,096 patients); sample sizes ranged from 51 to 184 patients. Eight trials were of high quality and two were low quality. Two trials did not report appropriate data, so were not included in the pooled analysis.

Corticosteroid treatment, compared with placebo, significantly reduced the time to clinically meaningful pain relief (WMD 4.54 hours, 95% CI 7.19 to 1.89; seven RCTs; $I^2=81\%$) and provided only a small reduction in pain scores at 24 hours (WMD 0.90 VAS, 95% CI 1.5 to 0.3; seven RCTs; $I^2=74\%$). However, high degrees of heterogeneity were identified for both pooled outcomes.

Subgroup analyses reported corticosteroid treatment in group A beta-haemolytic Streptococcus-positive patients was associated with a significant mean reduction in time to clinically meaningful pain relief (WMD 5.22 hours, 95% CI 7.02 to 3.42; $I^2=0\%$). Short-term side effect profiles between corticosteroids and placebo groups were similar. The primary results were not influenced by the use of fixed-effect compared with random-effects models, or by high-quality compared with low-quality trials. Corticosteroid treatment resulted in a small but significant reduction in the time to pain relief in the group A beta-haemolytic Streptococcus-positive subgroup.

Authors' conclusions
Despite the presence of significant heterogeneity, there was some evidence that corticosteroid administration for acute pharyngitis was associated with a relatively small effect on time to clinically meaningful pain relief and pain relief at 24 hours.

CRD commentary
This review answered a clearly defined research question. A search for both published and unpublished studies was performed with no language restrictions, so the risk of language and publication bias was likely to be low. However, the authors stated that to be included, studies had to mention 'placebo' in the title, abstract or indexing, but the inclusion criteria appeared to state that trials comparing corticosteroid to either placebo or to other alternative corticosteroids were eligible for inclusion. This appeared to suggest that relevant trials may have been missed during searching. The risk of reviewer error and bias was also likely to be low with regard to the selection of studies and assessment of methodological quality, but it was unclear whether similar precautions were taken when extracting the study data.

The methodological quality of the included trials was assessed using appropriate criteria; in general, quality was high in the most trials. Some characteristics of the trials were reported. Differences between the trials were identified, especially for the intervention regimens. The authors reported evidence of significant statistical heterogeneity between the trials. Some attempts were made to investigate the causes of heterogeneity, but the pooled effect sizes may not be reliable; this was acknowledged by the authors. The effect sizes were also reported as small and often not clinically significant.

Overall, the authors' acknowledged the limitations of the data and analyses, but their conclusions should be interpreted with appropriate caution, especially due to the risk of missing data.
Implications of the review for practice and research

Practice: The authors stated that the review does not support the routine use of corticosteroids for the treatment of acute pharyngitis potentially caused by group A beta-haemolytic *Streptococcus*. In patients with severe disease, physicians should weigh the risks and benefits of corticosteroids before instituting treatment.

Research: The authors did not state any implications for further research.

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