Glucocorticoids are ineffective in alcoholic hepatitis: a meta-analysis adjusting for confounding variables
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Authors' objectives
To perform a meta-analysis of controlled clinical trials of glucocorticoid treatment in alcoholic hepatitis, adjusting for prognostic variables and their possible interaction with therapy.

Searching
MEDLINE was searched and cross-bibliographic checks made of reference lists of published meta-analyses and individual trial reports. No details of the search strategy were given.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) that evaluated the effect of glucocorticoid treatment in the short term (less than 3 months) were eligible. Only those trials which provided a description of patient characteristics separately for both treatment groups were included.

Specific interventions included in the review
Glucocorticosteroid therapy versus placebo or no active drug control in patients with alcoholic hepatitis. The specific steroids used in the studies were: prednisolone, methylprednisolone and prednisone.

Participants included in the review
Patients with alcoholic hepatitis were included.

Outcomes assessed in the review
The outcome was mortality up to 2.5 months after randomisation.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
Each trial was rated using a published quality score. The authors do not state how the papers were assessed for quality, or how many of the authors performed the quality assessment.

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

Methods of synthesis
How were the studies combined?
The studies were combined by a meta-analysis using the DerSimonian and Laird method; the Woolf and Mantel-Haenszel methods were also used, but discounted due to the presence of statistically-significant heterogeneity between studies. The analysis was weighted by the sample size (specifically, the reciprocal of the variance).

How were differences between studies investigated?
Tests of heterogeneity of the relative risk (RR) were undertaken. Associations of mortality with descriptive variables...
were examined using weighted logistic regression.

**Results of the review**
Thirteen trials were identified (659 patients). However, not all trials were used in all stages of the meta-analyses. Twelve trials (622 patients) reported patient characteristics separately for each treatment group, and 11 trials reported further descriptive variables.

The pooled RR of death is 0.62 (95% CI: 0.38,1.05). The results using a fixed-effect model are statistically significant, showing a beneficial effect of glucocorticoid treatment.

The results are suggestive of publication bias; studies with a high weight (larger sample size) showing no therapeutic effect and those with a low weight (smaller sample size) showing an effect. No association was found between the effect size and the quality score, the type of corticosteroid, the daily dose or duration of therapy.

There was heterogeneity between trials, with the smallest trials having the greatest imbalance between treatment and control groups with respect to patient characteristics (age, male gender, encephalopathy, ascites, bilirubin and albumin). In particular, the following imbalance was associated with a high therapeutic effect: a low ratio of bilirubin, percentage male, or percentage with ascites.

Accounting for prognostic variables, the overall effect of glucocorticoid treatment is not significant - the RR is 0.78 (95% CI: 0.51,1.18). Poorer prognosis was significantly-associated with higher prevalence of encephalopathy and a high bilirubin concentration.

**Cost information**
No

**Authors' conclusions**
The overall effect of glucocorticosteroid treatment in patients with clinical alcoholic hepatitis is not statistically significant. Nevertheless, a beneficial or harmful effect cannot be excluded in some subgroups. New analyses of individual patient data from the largest trials are required, with the resultant hypotheses being tested in new randomised trials.

**CRD commentary**
There is a disparity between the reported inclusion criteria and the studies included in the meta-analyses. The results are presented both including and excluding one study which did not report sufficient detail to obtain patient characteristics in both groups. Insufficient detail is given in the paper about which studies reported what.

**Implications of the review for practice and research**
There is no evidence to support the routine use of glucocorticosteroids in the treatment of alcoholic hepatitis.

**Bibliographic details**

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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.