Corticosteroids in the prevention and treatment of acute respiratory distress syndrome (ARDS) in adults: meta-analysis

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CRD summary
This review aimed to assess the effectiveness of steroids in the prevention and treatment of acute respiratory distress syndrome (ARDS) in critically ill adults. The authors concluded that steroids started after the onset of ARDS may possibly reduce mortality. The authors' overall conclusions reflect the evidence presented and are likely to be reliable.

Authors' objectives
To assess the efficacy of steroids in the prevention of acute respiratory distress syndrome (ARDS) in critically ill adults, and the treatment of established ARDS.

Searching
MEDLINE, DARE, the Cochrane CENTRAL Register, the Cochrane Database of Systematic Reviews, ACP Journal Club and HTA were searched from 1966 to April 2007; the search terms were reported. Review articles were also screened to identify additional trials. The following journals were handsearched for papers and abstracts of conference proceedings: American Journal of Respiratory and Critical Care Medicine, Chest, Critical Care Medicine, European Respiratory Journal, Lancet, New England Journal of Medicine, Intensive Care Medicine and Thorax.

Study selection
Only randomised controlled trials (RCTs) evaluating steroid treatment compared with no steroid treatment to reduce the incidence of ARDS, or to improve the outcome from ARDS, in critically ill adults were eligible for inclusion. Studies of steroid use in fat embolism syndrome were excluded. The majority of patients had sepsis as a cause of ARDS. The mean age of all the participants was 52.2 years and 49% were male. Active treatment in the included studies consisted of methylprednisolone, hydrocortisone or dexamethasone.

Only trials reporting mortality, incidence of ARDS, or data on ventilation were included. A range of outcomes were reported and the primary outcome was hospital mortality or survival to hospital discharge.

Two reviewers independently assessed trials for inclusion.

Assessment of study quality
The quality of the studies was assessed using a 10-point scoring system modified from a previous meta-analysis. The criteria assessed were: randomisation; allocation concealment; blinding; definition of inclusion and exclusion criteria; similar baseline at study entry; protocol description; presence of cointervention; outcome definition; description of extent of follow up; and use of intention-to-treat analysis.

Three investigators assessed quality, with any disagreements resolved by consensus.

Data extraction
Data on the number of outcomes in the intervention and comparator groups were extracted, and odds ratios (ORs) and 95% credible intervals (CrIs) were calculated. For continuous outcomes, the mean difference and 95% CrIs were calculated.

Two investigators extracted predefined data from the included studies into standardised data extraction forms. Two investigators reviews and verified the extracted data before analysis.

Methods of synthesis
A Bayesian meta-analysis examining mortality, proportion of patients who developed ARDS, new infections, pneumonia and the number of ventilator-free days was performed using random-effects models. The studies were weighted, but the method of weighting was not stated. A Bayesian meta-regression was used to determine the relationship between the odds of mortality and time to treatment in ARDS, total dose of steroids, and year of study completion.

Heterogeneity was presented as the standard deviation (SD) between studies. A sensitivity analysis was undertaken in which the priors for the variability between studies were made less informative.

Publication bias was not formally assessed, owing to the small number of studies included.

**Results of the review**

Nine RCTs (n=1,073) were included in the review. Four studies evaluated the preventive use of steroids and 5 studies assessed steroid use after ARDS onset.

The trial quality scores ranged from 6 to 8 out of 10.

For studies examining preventive use, there was an 86.6% probability of an OR ≥1, suggesting evidence of an association between steroid therapy and the development of ARDS (OR 1.55, 95% CrI: 0.58, 4.05). There was also a weakly increased risk of death (72.8% probability of an OR ≥1) associated with steroid use in patients who went on to develop ARDS (OR 1.52, 95% CrI: 0.30, 5.94).

For studies examining therapeutic use, there was a 6.8% probability of an OR ≥1, suggesting that steroids were associated with a trend towards reduced mortality (OR 0.62, 95% CrI: 0.23, 1.26). Steroid therapy was associated with more ventilator-free days (mean difference 4.05 days, 95% CrI: 0.22, 8.71).

Heterogeneity was observed between the studies and was particularly evident in analyses looking at the development of pneumonia (SD=1.34).

The meta-regression showed a trend towards an increased number of patients developing new infections as the steroid dose increased, although no evidence of an association was found between odds of mortality and time to treatment, total steroid dose, or year of study completion. Further analyses were reported.

**Authors' conclusions**

Steroids started after the onset of ARDS may reduce mortality. Preventive steroids may possibly increase the incidence of ARDS in critically ill adults.

**CRD commentary**

The review addressed a clear question and was supported by appropriate inclusion criteria. Attempts to identify all relevant studies were undertaken by searching electronic databases and handsearching journals and conference proceedings. Despite the validity of the included studies being adequately assessed, these results were not used when interpreting the review analyses (e.g. none of the included studies described adequate procedures for allocation concealment). Comprehensive details of all the primary studies were provided, although the table on steroid dose and duration is difficult to interpret as there are no column headings. In addition, complex statistical analyses were used to pool the results and examine heterogeneity (although the method of weighting in the pooled analyses was not stated). The authors' overall conclusions reflect the evidence presented and are likely to be reliable.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that definitive treatment recommendations require further randomised trials or meta-analysis of individual patient data.
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