Effects of steroids on reintubation and post-extubation stridor in adults: meta-analysis of randomised controlled trials
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CRD summary
The authors concluded that IV steroids administered at least four hours prior to extubation had a beneficial effect on post-extubation stridor and reintubation in patients at high risk of stridor. The benefits were unclear for patients who were not at high risk of stridor. This was a generally well-conducted review. The authors’ conclusions are likely to be reliable.

Authors' objectives
To evaluate the effectiveness of prophylactic steroid therapy in preventing reintubation and post-extubation stridor in intubated adult patients.

Searching
PubMed, Cochrane Central Register of Controlled Trials (CENTRAL) and EMBASE were searched from January 1966 to November 2008. Search terms were reported. The search was expanded using the related articles tool. References of relevant articles, reviews and correspondence were handsearched. Abstracts of seven critical care meetings were searched from 2005 to 2008.

Study selection
Double-blind randomised controlled trials (RCT) that evaluated steroids administered prior to a planned extubation in patients with a mechanical ventilation of more than 24 hours were eligible for inclusion. The primary outcome of interest was incidence of reintubation. Secondary outcomes eligible for inclusion were post-extubation stridor, duration of intensive care unit stay and mortality. Studies that administered steroids for prevention of pulmonary fibrosis and studies of paediatric or neonatal patients were excluded.

Included RCTs were of methylprednisolone, hydrocortisone or dexamethasone administered intravenously in hydrocortisone equivalent overall doses that ranged from 100mg to 800mg in medical, surgical or trauma patients who underwent mechanical ventilation. Comparison groups received placebo. Where stated, mean duration of ventilation ranged from 4.6 days to 10.3 days. Three studies were only of patients at high risk of stridor.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the study selection.

Assessment of study quality
Methodological quality of the included studies was assessed using the Jadad scale of randomisation, blinding and completeness of follow-up (maximum score 5). Studies that scored 3 or more were eligible for inclusion.

Two reviewers independently assessed the methodological quality of the included studies. Disagreements were resolved through discussion or consultation with a third reviewer.

Data extraction
The number of events in each group was extracted and used to calculate relative risks (RR) with corresponding 95% confidence intervals (CI). Where the intervention group consisted of two or more separate arms, these were pooled into a single group. Authors of some studies were contacted for additional information.

The authors stated neither how data were extracted for the review nor how many reviewers performed the data extraction.
Methods of synthesis
Pooled RRs with corresponding 95% CIs were calculated using a Mantel-Haenszel-like method. Statistical heterogeneity was assessed using the Cochrane Q and $I^2$ statistics. Where there was significant statistical heterogeneity, a random-effects model was used. The number needed to treat and corresponding 95% CIs were calculated. Sensitivity analyses were performed for high-risk patients. Subgroup analyses were carried out for early versus late steroid administration. Funnel plots and Egger’s test were used to assess the presence of publication bias.

Results of the review
Seven double-blind RCTs were included for the review (n=1,846). Five RCTs received a Jadad score of 5 and two RCTs received a score of 3; two studies did not adequately describe randomisation procedure.

Treatment with steroids reduced the risk of reintubation by 42% compared to placebo (RR 0.58, 95% CI 0.41 to 0.81; seven RCTs, n=1,846; NNT=28). In high-risk patients, risk of reintubation was reduced by 62% (RR 0.38, 95% CI 0.21 to 0.72; three RCTs, n=279; NNT=9). Where studies did not select for risk, impact of steroids on risk of reintubation was less clear (RR 0.67, 95% CI 0.45 to 1.00; four RCTs, n=1,567).

Overall, steroid treatment was associated with a significant reduction in the risk of stridor (RR 0.48, 95% CI 0.26 to 0.87; seven studies, n=1,846). However, there was significant statistical heterogeneity ($p<0.0001$) and when an outlying trial was removed the advantage of steroid treatment disappeared. Steroid treatment was associated with a significant reduction in the risk of stridor in patients at high risk of stridor, (RR 0.40, 95% CI 0.25 to 0.63; three RCTs, n=279), but not when patients were not selected for risk of stridor.

When steroids were administered early (four to 24 hours prior to extubation), they significantly reduced the risk of reintubation (RR 0.55, 95% CI 0.32 to 0.94; two RCTs, n=796). Late administration of steroids (less than two hours before extubation) did not significantly affect the risk of reintubation.

The funnel plot showed no evidence of publication bias.

Authors' conclusions
Steroids had a beneficial effect on the prevention of post-extubation stridor and reintubation in patients at high risk of stridor where IV steroids are administered at least four hours prior to extubation. The benefits were unclear for patients who were not at high risk of stridor.

CRD commentary
The review addressed a clear question with well-defined inclusion criteria. Three relevant data bases were searched. Attempts were made to search for unpublished material. Publication bias was assessed and no evidence of it found. It was unclear whether language restrictions were applied to the search, so language bias could not be ruled out. A suitable tool was used to assess methodological quality of included studies, only good-quality studies were included and appropriate steps were taken in the validity assessment to minimise reviewer error and bias. However, it was unclear whether similar steps were taken in study selection and data extraction processes, so reviewer error and bias could not be ruled out definitively. Appropriate methods were used to combine data. Statistical heterogeneity was assessed. Despite some omissions in the reporting of methods used, this was a generally well-conducted review and the authors’ conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that it was recommended to start steroid treatment at least four hours before planned extubation.

Research: The authors stated that further research was needed to determine the optimal steroid route, type, dosing regimen and duration in patients at high risk of stridor. Further research was needed into use of steroids in patients who were not selected for high risk and into the potential adverse effects of steroid use.

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