Prophylactic administration of parenteral steroids for preventing airway complications after extubation in adults: meta-analysis of randomised placebo controlled trials


CRD summary
This well-conducted review concluded that prophylactic administration of parenteral steroids before planned extubation is effective in reducing the incidence of laryngeal oedema and subsequent reintubation rates in adults. The results should be interpreted with caution due to limitations within the primary data.

Authors' objectives
To review the effectiveness of parenteral steroids in preventing laryngeal oedema after extubation and reducing the need for subsequent reintubation in critically ill adults.

Searching
The following databases were searched from inception to June 2008: PubMed, CENTRAL, Web of Science, EMBASE. Search terms were reported and a filter for the detection of randomised controlled trials (RCTs) was used. Reference lists of review articles and included publications were searched for additional studies. No limits were placed on language, year of publication or publication status.

Study selection
Only randomised placebo controlled trials (RCT) were eligible for inclusion. The intervention of interest was prophylactic steroids compared with placebo prior to planned extubation in adults. Studies were included if they reported on the occurrence of laryngeal oedema defined as the presence of stridor and dyspnoea (minor laryngeal oedema) after extubation or severe respiratory distress (major laryngeal oedema) leading to subsequent reintubation. Secondary outcomes included the number of consequent reintubations.

Included studies were all placebo controlled RCTs and used single or multiple doses of a parenteral steroid: methylprednisolone, dexamethasone or hydrocortisone. Study participants were all adults who had been tracheally intubated for at least 24 hours and who were monitored for at least 24 hours following extubation. All studies reported both presence of laryngeal oedema and rate of subsequent reintubation. Studies were selected by two reviewers; it was unclear how discrepancies were resolved.

Assessment of study quality
Included studies were assessed for quality based on allocation concealment (judged as adequate, uncertain or clearly inadequate) and by using the Jadad 5-point scale, which considers randomisation, masking and reporting of drop-outs and withdrawals. Quality assessment was performed in duplicate by two independent reviewers and any disagreements were resolved by consensus.

Data extraction
Data on rates of laryngeal oedema and reintubation were extracted as dichotomous variables and odds ratios (OR) with associated 95% confidence intervals (CI) calculated for each primary study. For the analysis of dose relationships all steroid doses were converted to the equivalent dose of methylprednisolone. Data were extracted in duplicate by two independent reviewers and any disagreements were resolved by consensus.

Methods of synthesis
Data were pooled where possible using fixed-effects meta-analysis to produce pooled ORs and 95% CIs for the primary and secondary outcomes. Heterogeneity was assessed using the Q statistic, $\chi^2$ and $I^2$ where the Q-statistic was significant ($p < 0.1$) a random-effects model was used. Subgroup analyses were carried out on dose regimen (single or multiple). Sensitivity analyses were used to explore possible sources of heterogeneity. A funnel plot was used to check for publication bias. Risk differences, number needed to treat (NNT) to benefit one patient and power of each analyses were also calculated.
Results of the review
A total of six RCTs were included (n=1,923, samples ranged from 38 to 381) in this review; three undertaken in Asia and three in Europe. A total of 984 patients received steroids and 939 received placebo. Most of the studies were of high quality (Jadad scores of 3 or better) with all except one clearly reporting allocation concealment (although few trials reported intention to treat analyses). Two trials mentioned using additional supportive treatments to reduce laryngeal oedema that may have influenced the results. The funnel plot was described as asymmetrical (not shown).

Laryngeal Oedema:
A fixed-effects meta-analysis of all six RCTs found that prophylactic steroids reduced laryngeal oedema after extubation, but the Q test indicated significant heterogeneity between studies. A random-effects analysis supported the initial result with a smaller effect estimate OR 0.38 (95% CI: 0.17, 0.85; p=0.02) which corresponded to an absolute risk difference of -0.10 (-0.20 to 0.00) and a NNT of 10. Subgroup analyses of three RCTs (n=863) suggested that there was a significant benefit from multiple dose regimen(s) in the reduction of laryngeal oedema OR 0.14 (95% CI: 0.08, 0.23) corresponding to a reduction of -0.19 (-0.24, -0.15) in absolute risk difference and NNT of 5. Analysis of the four single dose regimen trials (n=1,103) showed a non-significant trend towards benefit.

Reintubation:
A fixed-effects meta-analysis of all six RCTs (no significant heterogeneity) gave an OR 0.29 (95% CI: 0.15, 0.58) with a reduction in absolute risk of -0.02 (-0.04, -0.01) and a NNT of 50. Subgroup analyses of three RCTs (n=863) suggested that there was a significant benefit from multiple dose regimen(s) in the reduction of reintubation rates OR 0.19 (95% CI: 0.07, 0.50) corresponding to a reduction of -0.04 (-0.07, -0.02) in absolute risk difference and NNT of 25. Analysis of the four single-dose regimen(s) trials (n=1,103) showed a non-significant trend towards benefit.

Adverse Events:
Three trials (n=969) reported data but could not be pooled. In the steroid group two patients suffered adverse events not considered to be related to the intervention. In the placebo group one patient developed respiratory failure.

Sensitivity analyses based on trial quality did not affect the results. Further analyses are reported in the full paper.

Authors’ conclusions
Prophylactic administration of multi-dose regimen parental steroids before planned extubation is effective in reducing the incidence of laryngeal oedema and subsequent reintubation rates in adults, with an infrequent incidence of adverse events.

CRD commentary
This was a well-conducted review that followed good practice guidelines for systematic reviewing. The review is likely to have minimised both reviewer error and potential bias at all stages. The inclusion criteria were clear and the searches relatively comprehensive without restrictions on language. The authors identify the possibility of publication bias (asymmetric funnel plot), but it is unclear how much this might have affected the results. Included studies were assessed for validity using an established tool, and the majority of studies were rated as high quality. The authors acknowledged that sample sizes were small and many of the confidence intervals were wide. The analyses were appropriate and took heterogeneity into account. Overall the conclusions from this review should be interpreted with caution due to the small number of included studies and variation in their results.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further trials are required to establish the optimal dose of steroids and the optimal time between start of treatment and planned extubation.

Funding
Bibliographic details

PubMedID
18936064

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Critical Illness /therapy; Device Removal /adverse effects; Humans; Infusions, Parenteral; Intubation, Intratracheal /adverse effects; Laryngeal Edema /prevention & control; Randomized Controlled Trials as Topic; Respiration, Artificial /adverse effects; Retreatment; Steroids /administration & dosage; Treatment Outcome; Ventilator Weaning /adverse effects

AccessionNumber
12008106510

Date bibliographic record published
01/12/2008

Date abstract record published
02/03/2009

Record Status
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.