Do corticosteroids reduce the risk of fat embolism syndrome in patients with long-bone fractures? A meta-analysis

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CRD summary
This well-conducted systematic review of seven trials found that corticosteroids may be beneficial in preventing fat embolism syndrome and hypoxia in patients with long-bone fractures. The authors' conclusions are based on the evidence, but small sample sizes, randomisation failures and lack of generalisability to a modern multiple trauma setting engender some uncertainty in the reliability of the conclusions.

Authors' objectives
To determine the effect of corticosteroids on the risk of fat embolism syndrome in patients with long-bone fractures.

Searching
MEDLINE, EMBASE, HealthSTAR, CINAHL and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1966 to September 2006 with no language restrictions. Search terms were reported. Seven major orthopedic journals were handsearched for the same period, as were abstracts of three major meetings. References of included studies were also assessed for eligibility.

Study selection
Randomised and quasi-randomised trials of patients with at least one long-bone fracture that compared prophylactic corticosteroid intervention with no pharmacological treatment. Trials were excluded where patients had clinically important associated head, chest or abdominal injuries.

The primary outcome was fat embolism syndrome based on the respiratory, neurological and cutaneous manifestations defined in the individual trials, and by presence of hypoxia as confirmed by arterial blood gas measurement and the presence of classic petechial rash. Secondary outcomes were mortality, major infective complication and avascular necrosis within the follow-up period. Results were also presented for petechiae, but this was not explicitly defined as a secondary outcome.

Patients in included trials were predominantly male, with mean age ranging from 22 to 42 years.

Two reviewers independently assessed the studies for inclusion and disagreements were resolved by two other reviewers.

Assessment of study quality
Validity assessment was based on randomisation method and blinding of outcome assessors in addition to the use of a 21-point quality assessment scale converted to a score out of 100.

Two reviewers independently assessed study validity with two further reviewers verifying the initial assessments.

Data extraction
Two reviewers independently extracted binary (dichotomous) outcome data to generate risk ratios (RR), absolute risk differences, numbers needed to treat (NNT) and associated 95% confidence intervals (CIs). Effect moderators based on dose (more or less than 20mg/kg) and quality (higher or lower than 50 on a 100 point converted scale) were also extracted.

Extraction was undertaken by two independent reviewers.
Methods of synthesis
Effect sizes were pooled for each outcome using an unspecified random-effects model. Statistical heterogeneity was tested using the Breslow-Day test and measured using $I^2$.

Subgroup analyses were performed for dose, quality score, degree of blinding and randomisation.

Visual assessment of funnel plots was used to assess publication bias.

Results of the review
Six trials (389 patients) reported the primary outcome, with a further trial reporting mortality. Sample size ranged from 20 to 87 patients. There was considerable variation in both quality (two trials were quasi-randomised) and the dose and duration of corticosteroid treatment.

Corticosteroids reduced the risk of fat embolism syndrome by 78% (RR 0.22, 95% CI 0.08 to 0.57; NNT 8, 95% CI 5 to 13). The authors stated that funnel plots (not presented) did not suggest publication bias.

Corticosteroids also reduced the risk of hypoxia by 61% (RR 0.39, 95% CI 0.21 to 0.71), but did not have a statistically significant effect on petechiae, mortality or infection. No trials measured avascular necrosis.

There were no significant differences between subgroups based on dose, quality score, degree of blinding or randomisation.

Heterogeneity between trials was not statistically significant in any of the analyses.

Authors' conclusions
Evidence suggested that corticosteroids may be beneficial in preventing fat embolism syndrome and hypoxia, but not mortality, in patients with long-bone fractures without increased risk of infection. A large RCT is required to corroborate the results of this meta-analysis.

CRD commentary
The review question was well defined and supported by appropriate inclusion criteria. The literature search was comprehensive and replicable. The authors undertook screening, validity assessment and data extraction in duplicate minimising potential biases. Previously published criteria were used to assess trial quality.

The random-effects analysis of primary and secondary outcomes was appropriate. Subgroup analyses were also appropriate, but lacked power. Formal tests of statistical heterogeneity were reported. The authors acknowledged limitations with the included studies, such as their quality and heterogeneity in definitions of fat embolism syndrome and intervention delivery. They also noted that the trials (and patients within them) may not be representative of a multiple trauma setting with modern nailing techniques, perioperative protocols and low dose protocols.

Given these limitations, the authors' conclusions, implications for further work and caution regarding changes to current practice, are appropriate.

Implications of the review for practice and research
Practice: The authors stated that no change in current practice is recommended

Research: The authors stated that a large randomised trial is required to assess the efficacy of corticosteroids in the multiple trauma setting with modern nailing techniques, perioperative and low dose protocols and a standard definition of fat embolism syndrome.

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