Efficacy of prophylactic antibiotic therapy in spinal surgery: a meta-analysis

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Authors' objectives
To examine the efficacy of prophylactic antibiotic treatment in spinal surgery.

Searching
A primary search was undertaken in MEDLINE (1966 to October 2000); further details, including search terms, were reported. Additional searches were undertaken in MEDLINE and the Cochrane Controlled Trials Register. The reference lists of textbook chapters, review articles, and the articles retrieved from the primary search were also examined.

Study selection
Study designs of evaluations included in the review
The inclusion criteria specified that randomised controlled trials (RCTs) were eligible. Data from non-randomised trials were also reported.

Specific interventions included in the review
Comparisons of prophylactic antibiotic therapy and no therapy were eligible.

Participants included in the review
Patients who underwent spinal operations were eligible. Studies that included subgroups of such patients within trials involving patients undergoing general neurosurgical or orthopaedic procedures were also eligible.

Outcomes assessed in the review
The inclusion criteria were not defined in terms of the outcome, but studies that did not report specific information on wound infections were later excluded. The primary outcome of interest was the wound infection rate after surgery.

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

Assessment of study quality
The author does not report a formal method for assessing validity, but aspects of study quality such as allocation and blinding were discussed.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The wound infection rate was calculated as a conditional maximal likelihood odds ratio for each study.

Methods of synthesis
How were the studies combined?
The studies were primarily combined using a random-effects model. The authors also presented data combined using a fixed-effect model, and undertook a Bayesian meta-analysis to test for potential bias in the analyses. The author also carried out a cumulative meta-analysis using a fixed-effect model. Funnel plots and Rosenthal's test were used to test for publication bias.
How were differences between studies investigated?
Homogeneity was assessed using Cochran's Q test. The author performed a sensitivity analysis to investigate the effect of including pseudo-randomised trials. An analysis of six non-randomised studies was also performed.

Results of the review
Four RCTs and two pseudo-RCTs (n=843) were included in the meta-analysis. A further six non-randomised studies could not be included in the primary meta-analysis.

Lower wound infection rates for antibiotic-treated patients were reported in all six trials. However, the results were not statistically significant for any individual study. Combining the studies in a random-effects model demonstrated a significant effect in favour of antibiotic prophylaxis; the pooled odds ratio (OR) was 0.37 (95% confidence interval, CI: 0.17, 0.78, p<0.01). There was no evidence of statistical heterogeneity (p>0.98). The use of risk differences gave a difference of 2.9% in favour of antibiotic therapy, giving a number-needed-to-treat of 34 patients to prevent one infection. The results from meta-analyses using a fixed-effect model and Bayesian methods gave essentially identical results.

The results of the fixed-effect cumulative meta-analysis showed that the pooled OR became significant at the p<0.05 level in 1990 and at the p<0.01 level in 1994, the date of the last trial to be published.

The author states that the results of the funnel plot and Rosenthal's test indicated that there was no evidence of publication bias.

The sensitivity analyses showed that the exclusion of pseudo-randomised trials from the meta-analysis produced essentially identical results to the main analysis.

There was no evidence of different treatment effects with different dosing periods or with the inclusion of Gram-negative coverage (i.e. antibiotics with both Gram-negative and -positive coverage as opposed to Gram-positive coverage alone). There was considerable heterogeneity in the infection rates, which suggested differences in baseline infection risks between the trials. This finding was investigated using a Bayesian meta-regression. The model indicated no evidence for a dependence of the treatment effect on the control arm infection rate.

Non-randomised trials (6 studies, n=6,930): the pooled OR showed significantly lower infection rates in the prophylactic antibiotic therapy group (OR 0.22, 95% CI: 0.15, 0.33, p<0.001). There was no significant evidence of heterogeneity (p=0.76). The results of the pooled OR were dominated by a single large trial. The author states that the funnel plot showed evidence of publication bias.

Authors' conclusions
The meta-analysis of RCTs provided clinically and statistically significant evidence that prophylactic antibiotic therapy for spinal operations is effective under a wide range of clinical conditions with various antibiotic regimens.

CRD commentary
On the whole, the methodological quality of this review was satisfactory. The review question was appropriate. However, although the inclusion and exclusion criteria could be found within the text of the review, they were not clearly set out. Full details of the search strategy were reported in the paper. However, only two databases were searched and, although the strategy appeared to be thorough, some important studies may have been missed. Details of the review process, such as the number of reviewers who carried out the study selection and data extraction processes, were not reported. Aspects of the quality of the included RCTs were discussed, but the author did not report using a published checklist to assess their validity. Selected study details were tabulated. The methods used to pool the data were appropriate and several different techniques were used. The main analyses were undertaken using a random-effects model and heterogeneity was also evaluated with statistical testing. The author's conclusions follow from the data presented.
Implications of the review for practice and research

Practice: The author states that taken together, these results strongly support the practice of administering at least a single pre-operative dose of an antibiotic active against Gram-positive organisms for spinal operations. The author also states these results suggest wide applicability to most clinical situations in spinal surgery.

Research: The author states that future trials of antibiotic prophylaxis in spinal surgery should use an active control arm, rather than placebo treatment.

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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.