Ceftriaxone versus other cephalosporins for perioperative antibiotic prophylaxis: a meta-analysis of 43 randomized controlled trials

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Authors' objectives
To compare the efficacy of ceftriaxone versus other cephalosporins in the peri-operative prophylaxis of surgical wound, urinary tract and respiratory tract infections.

Searching
MEDLINE, EMBASE, SIGLE, ROPU (Hoffmann-La Roche internal database), DHSS Data, and MEDIKAT were searched for English, French and German literature published between January 1, 1986 and December 31, 1996. The search terms were not stated in the article. Studies reported in more than one publication were included as single studies.

Study selection
Study designs of evaluations included in the review
The inclusion criteria for study design specified open or blind randomised studies of any sample size.

Specific interventions included in the review
Comparisons of ceftriaxone with another cephalosporin (cefamandole, cefazolin, cefotaxime, cefotiam, cefoxitin and cefuroxime) were eligible for inclusion. The antibiotics in the included studies could be used once or several times in elective or emergency surgery, and were allowed to be used in combination with anti-anaerobic antibiotics. Studies involving bowel preparations were included only if the preparation did not include an antibiotic, or if the same antibiotic was used in both study arms. Other forms of bowel preparation were considered equivalent.

Participants included in the review
Studies in adult patients undergoing peri-operative antibiotic prophylaxis were eligible for inclusion.

Outcomes assessed in the review
Specific inclusion criteria for the outcomes were not pre-specified, but any definition of infection was included. The outcome used in the review was infection rates in post-operative wounds, urinary tract infections and respiratory tract infections.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the articles for inclusion. A third reviewer was consulted if there were any discrepancies.

Assessment of study quality
The authors used the Jadad quality scoring scale (range: 0 to 5) to group the studies into three groups (0 to 1, 2, and 3 to 5); a score of 1 indicated low quality and a score of 5 indicated high quality. The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. Details of the data extracted from the included studies were not reported.

Methods of synthesis
How were the studies combined?
Where two cephalosporins were compared with ceftriaxone, these were compared together providing that they had the same in vitro spectrum. A separate meta-analysis was performed for each type of infection (surgical wound, urinary tract and respiratory tract infection) using random-effects and fixed-effect models. The infection rates were compared using the relative risk (RR). A 98.3% confidence interval (CI) was calculated for each pooled RR. Funnel plots were used to investigate the possibility of publication bias.

How were differences between studies investigated?
Tests for homogeneity were performed, although the statistical tests used were not named. A sensitivity analysis was also performed to determine whether the results in studies with infections meeting Centers for Disease Control and Prevention (CDC) criteria were similar to those not employing this definition. The CDC-compliant studies were further analysed using four parameters: type of surgery; monotherapy or combination therapy; quality score; and blinding.

Results of the review
Sixty studies met the inclusion criteria, but only 43 (n=13,482) were included in the analyses. The reasons for excluding the 17 studies were not stated.

Postoperative wound infections (40 studies with 13,303 participants).

The RR was 30% lower in the ceftriaxone group versus the control group (RR 0.70, 98.3% CI: 0.55, 0.89, p=0.0002), and the individual study results were found to be homogeneous. The funnel plot analysis did not indicate publication bias. In the CDC-compliant subgroup (n=29 studies), the RR was 0.74 (CI not stated).

Urinary tract infections (24 studies with 8,865 participants).

The RR was 47% lower in the ceftriaxone group versus the control group (RR 0.53, 98.3% CI: 0.43, 0.67, p<0.0001), and the individual study results were found to be homogeneous. In the CDC-compliant subgroup (n=8 studies), the RR was 0.63 (98.3% CI: 0.36, 1.12), indicating no statistically-significant difference (p=0.055).

Respiratory tract infections (25 studies with 9,567 participants).

The RR showed no statistically-significant difference between ceftriaxone and controls (RR 0.81, 98.3% CI: 0.61, 1.09, p=0.04). Results for the CDC-compliant subgroup analysis (n=10 studies) also showed no statistically-significant differences. The individual study results were found to be homogeneous.

Authors’ conclusions
The authors state that this meta-analysis shows that ceftriaxone is statistically significantly superior to other cephalosporins in preventing post-operative wound infections. However, the trend towards lower post-operative urinary tract infection rates needs confirmation in further randomised studies.

CRD commentary
The authors clearly stated the research question, and the inclusion and exclusion criteria were adequate. The literature search covered several databases and was not restricted to English language publications. The search terms were not stated and there was no stated attempt to find unpublished or grey literature, although the authors found no evidence for publication bias.

The quality of the included studies was formally assessed. The authors used the results of this quality assessment to group the studies for further analyses, to see whether quality affected the statistical outcomes, although the results of these analyses were not reported.

The authors’ only positive conclusion was that ceftriaxone is more effective than other cephalosporins at preventing post-operative wound infection. This was based on a fixed-effect pooling of 40 (or 29 CDC-defined outcome) different trials. The treatment and control regimens used in those studies were not reported. Therefore, the appropriateness of
pooling the studies to obtain an average treatment effect is questionable (regardless of statistical homogeneity). It is noteworthy that this was the only outcome for which the random-effects analysis, which would be expected to provide a more conservative and perhaps not statistically-significant result, was not shown.

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

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

Research: The authors state that further randomised studies with clear and comparable microbiological and clinical criteria to define urinary tract infection should be performed. They also state that the cost-effectiveness of treatment regimes should be analysed in future studies.

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