Fluoroquinolones versus beta-lactam based regimens for the treatment of osteomyelitis: a meta-analysis of randomized controlled trials

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CRD summary
This review compared fluoroquinolones with beta-lactams for the treatment of osteomyelitis. The authors concluded that the two treatments were equally effective. Although the review was generally well conducted, limitations in the available evidence and reporting of the review mean that the conclusion of equivalence may not be reliable.

Authors' objectives
To compare fluoroquinolones with beta-lactams for the treatment of osteomyelitis.

Searching
PubMed and the Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched for relevant evidence. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) that compared fluoroquinolones with other conventional agents for the treatment of patients with osteomyelitis were eligible for inclusion in the review. Eligible trials also had to include a minimum of 10 patients in each treatment arm and report data on clinical success (the primary review outcome), bacteriological success, relapses, and super-infections and/or adverse events.

Among selected trials, fluoroquinolones included ofloxacin, ciprofloxacin, and pefloxacin. Comparators among the included trials all included beta-lactams (imipenem/cilastatin, ampicillin/sulbactam, amoxicillin/clavulanic, cefazoline or cefazidime, broad spectrum cephalosporin or nafcillin-aminoglycoside, parental therapy with beta-lactams, or other appropriate antimicrobial therapy). Most trials were in patients with chronic osteomyelitis; some trials also included patients with acute osteomyelitis. The authors stated that most trials did not report details of the location of osteomyelitis or surgical procedures performed during the trial period.

Two reviewers independently selected studies for inclusion, with disagreements resolved by consensus among all review authors.

Assessment of study quality
Quality of included trials was assessed according to the Jadad scale that allocated trials a score of 0 to 5 based on reporting of randomisation, blinding, and withdrawals. Trials that received a score greater than 2 were considered to be good quality.

Two reviewers independently assessed validity.

Data extraction
Data were extracted to allow the calculation of odds ratios (ORs) and related 95% confidence intervals (CIs) for each outcome.

Two reviewers independently extracted data from included studies.

Methods of synthesis
Pooled odds ratios and 95% confidence intervals were calculated for each outcome using both the Mantel-Haenszel fixed-effect model and the DerSimonian-Laird random-effects model. Statistical heterogeneity was assessed using the $\chi^2$ test. In the absence of heterogeneity, the results of the fixed-effect model were presented; otherwise the random-
Results of the review
A total of seven RCTs (n=411 patients) were included in the review. Five trials received a score of 2 points on the Jadad validity scale, with the remaining trials receiving 1 point and 3 points. Where reported, the duration of follow-up ranged from six to 18 months.

There was no statistically difference between fluoroquinolones and beta-lactams for clinical treatment success (OR 0.99, 95% CI 0.51 to 1.91; seven RCTs; 194 patients). Also, there were no statistically significant differences between the treatments for bacteriological success (six RCTs; n=201 isolates), super-infections (six RCTs; n=173 patients), relapses (five RCTs; n=153 patients) or adverse events (five RCTs; n=170 patients). The authors did not state why the number of patients analysed appeared to be considerably lower than the number of patients enrolled.

Authors' conclusions
Fluoroquinolones were as effective as beta-lactams for the treatment of osteomyelitis.

CRD commentary
The review question was clearly defined in terms of study design, participants, interventions, comparators and outcomes of interest. Attempts were made to minimise bias and error at each stage of the review process. However, it was not clear if attempts were made to identify unpublished or non-English language trials, so bias resulting from missing such trials could not be ruled out. Established methods were used to syntheses and assess the quality of included studies.

The authors assessed the validity of included trials; all had limitations, withdrawal rates (in particular) appeared to be high. The number of patients analysed appeared to be considerably lower than the number of enrolled patients; the reason for this discrepancy was not clear. In addition, included trials were conducted between 1987 and 1991, and the total number of patients was small, particularly for establishing equivalence between two treatments. Therefore, the authors' conclusion may not be reliable.

Implications of the review for practice and research
Practice: The authors stated that, since they can be administered in the outpatient setting, fluoroquinolones appear to be a valid alternative for the long-term treatment of osteomyelitis, although they should be used with caution to preserve their activity against increasingly resistant bacteria.

Research: The authors did not state any implications for research.

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