Antimicrobial prophylaxis in total hip replacement: a systematic review

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Authors' objectives
To assess the comparative efficacy and cost-effectiveness of antimicrobial prophylaxis used for patients undergoing a total hip replacement (THR).

Searching
The authors searched the electronic databases MEDLINE, EMBASE and the Cochrane Controlled Trials Register up to November 1998 using a search strategy developed by the Centre for Reviews and Dissemination at York University. The authors also scanned the reference lists of existing reviews and experts in the field were also contacted to help identify further studies. There were no language restrictions.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs).

Specific interventions included in the review
Antimicrobial prophylaxis versus no antimicrobial prophylaxis or placebo administered at the time of THR surgery. Included antimicrobials were cefonicid, cefoperazone, ceforanide, cefotaxime, cefoxitin, cefuroxime, cephalothin, cefamandole, cephazolin, cephradine, cloxacillin, gentamicin, lincomycin, teicoplanin and ticarcillin/clavulanic acid. The type of operating theatre (conventional/ultraclean) was also recorded with the intervention.

Participants included in the review
Patients undergoing an elective THR (either primary THR (replacement of the femoral head and the acetabulum) or revision THR (replacement of the acetabular or femoral components, or both, following the failure of a primary THR) regardless of protheses used. Patients in whom the principal diagnosis was infection of the hip were excluded from the review. Trials examining antimicrobial prophylaxis in both THR and TKR patients were included, with the results for THR analysed separately where possible.

Outcomes assessed in the review
Primary outcome measure was wound infection, either:

1. Major deep wound infection, a deep surgical wound infection (SWI) occurring at the incision site within one year and involving tissues or spaces at or beneath the fascial layer.

2. Minor superficial wound infection, an infection occurring at the incision site within 30 days after surgery, involving the skin, subcutaneous tissue, or muscle located above the fascial layer. Late prosthetic infections (up to one year following surgery) were also recorded.

Secondary outcome measures were: mortality related to infection; systemic infection (e.g. septicaemia); remote infection (e.g. urinary tract and respiratory tract infections); adverse effects; and resource use outcomes (e.g. length of hospital stay, re-operation, postoperative antibiotic therapy).

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed the studies for inclusion. Discrepancies were resolved through discussion.

Assessment of study quality
Studies were assessed using the following items: method of randomisation; a priori calculation of sample size; analysis on an intention-to-treat basis; assessment of outcome blinded; groups comparable at baseline; inclusion/exclusion...
criteria clearly defined; method of assessment of wound infection; and duration of follow-up. These items were scored using an adaptation of the system used by the Cochrane Musculoskeletal Injuries Group. Trials meeting the inclusion criteria were assessed for validity by one reviewer and checked by a second. Discrepancies were resolved through discussion with a third reviewer.

Data extraction
Data were extracted by one reviewer using a predefined data extraction form. The data were checked for accuracy by a second reviewer. If disagreements could not be resolved through discussion they were taken to a third party.

Data were extracted for the categories of: study identification, year of publication and results of validity assessment, patient characteristics (numbers, age, sex) and definition of infection, antibiotic regimen, results, and comments and authors' conclusions. Cost-effectiveness data were also recorded though no further analysis was undertaken on these data.

Methods of synthesis
How were the studies combined?
Studies were grouped and analysed by type of antimicrobial intervention. Where sufficient data were available pooled relative risk (RR) with 95% confidence intervals (CIs) and number-needed-to-treat (NNT) were calculated using a fixed-effect model.

How were differences between studies investigated?
Heterogeneity was assessed using the chi-squared statistic (Revman software). Sub-group analyses, where possible, were conducted according to the nature of the THR (i.e. primary or revision procedure) and the type of prosthesis.

Results of the review
Twenty-five RCTs were included in the review with 15,283 participants. The number of patients randomised to a treatment arm within a trial ranged from 18 to 1,600, with nearly half of all trials recruiting less than 100 participants.

In five trials comparing antibiotics to placebo for the prevention of SWIs: SWI rate 1.0% versus 4.3%; RR 0.24, 95% CI: 0.14, 0.43; NNT 30.

In 15 other comparisons of antimicrobial versus antimicrobial, it was not possible to identify the most effective antimicrobial agent within the review.

Route of administration: gentamicin-loaded bone cement (1 RCT) was statistically significantly better than systemic antimicrobial prophylaxis (RR 4.38, 95% CI: 1.25, 15.32) while systemic antimicrobial prophylaxis was better than cefuroxime-loaded bone cement (1 RCT) (RR 0.51, 95% CI: 0.24, 1.06) although this was not statistically significant.

Twelve of the 25 trials reported adverse effects such as nausea, vomiting, erythema on administration of antibiotic, gastric pyrosis, cutaneous rash and mild dyspnoea. No serious toxicity or adverse events were reported in any trial.

Cost information
Six trials provided information on costs, although these should be viewed with caution because of incomplete measures of cost and benefit and the fact that the most recent studies had been published in the USA (and therefore not directly applicable to the UK).

Authors' conclusions
The authors state that antimicrobial prophylaxis is effective for the prevention of SWI in both total knee replacement (TKR) and THR surgery. The efficacy of many of the regimens studied may be similar, and available data make it difficult to identify an optimal regimen. There is no convincing evidence to suggest that the new-generation cephalosporins are more effective at preventing postoperative SWI infections in THR/TKR surgery than the first-
generation cephalosporins. Similarly, there is no convincing evidence to suggest that extending the duration of a regimen beyond 24 hours postoperatively reduces the number of SWI following THR/TKR surgery. Single-dose of short-term administration is not only as effective as long-term administration, but will lower overall costs and may reduce the risk of toxicity and the development of bacterial resistance.

**CRD commentary**

This was a good review. The authors have clearly stated the research question and inclusion and exclusion criteria. The literature search appears to be thorough. The authors also include searches for unpublished and grey literature. The quality of the included studies was formally assessed and discussed in the review. The authors have reported how the articles were selected, and who performed the selection, and the validity assessment and data extraction.

The data extraction is reported in tables and discussed in the text of the review. The studies were combined in a statistical meta-analysis where possible and narratively otherwise using a fixed-effect model. Tests for heterogeneity were made but the results are not reported, hence it is not known whether the trials of antimicrobials versus placebo should have been combined.

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

**Practice:** Although there is evidence to support the use of antimicrobial prophylaxis in elective THR, the universal acceptance of a fixed antimicrobial regimen should be avoided to minimise the development of antibiotic-resistant bacteria.

**Research:** The authors state that no further small, underpowered trials examining antimicrobial prophylaxis for the prevention of SWI following THR/TKR should be funded. Further, it may not be cost-effective to carry out mega-trials. Rather, future research needs to examine the risk factors that determine the level of SWIs in patients undergoing THR, although these trials need to have sufficient power and assess the issues of validity highlighted in this review.

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