Single- versus multiple-dose antibiotic prophylaxis in the surgical treatment of closed fractures: a meta-analysis
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CRD summary
The authors concluded that multiple-dose perioperative antibiotic prophylaxis was not more effective than a single preoperative dose for preventing surgical wound infections during the treatment of closed long bone fractures. Given some shortcomings in the review process, the uncertain quality of included trials and variability across antibiotics and dosing schedules, the authors’ conclusions should be interpreted with caution.

Authors' objectives
To determine if multiple-dose perioperative antibiotic prophylaxis is more effective than a single preoperative dose in the prevention of surgical wound infections during the treatment of closed long bone fractures.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), and the Cochrane Database of Systematic Reviews were searched without language restrictions to October 2006; search terms were reported. Additional studies were sought through relevant conference proceedings: Canadian Orthopaedic Association, American Academy of Orthopedic Surgeons, Orthopaedic Trauma Association, British Orthopaedic Association and the European Federation of National Associations of Orthopaedics and Traumatology. References of selected studies were also searched.

Study selection
Prospective randomised controlled trials (RCTs), or quasi RCTs were eligible if they compared a single preoperative prophylactic dose of antibiotic with a multiple-dose perioperative strategy for the treatment of closed long bone fractures using internal surgical fixation or arthroplasty. Trials of open fractures were excluded. Eligible trials had to report the primary outcome of wound infection.

All fracture types or hip fractures were assessed in the included trials. Included trials evaluated the following antibiotics: cefazolin, cefamandole, cefonicid, cefotaxime, ceftazidime, ceftriaxone and cefuroxime; dosing schedules and half-lives varied. Trials compared single-dose regimens with multi-dose regimens, mostly consisting of three or more doses every eight hours. The mean age of participants ranged from 26 to 77 years; just under two-thirds of patients were female.

Two reviewers independently selected potential studies and three reviewers independently selected studies for inclusion in the review.

Assessment of study quality
The authors did not state that they performed a validity assessment.

Data extraction
An independent statistician extracted wound infection rates and converted these to risk ratios.

Methods of synthesis
Risk ratios and risk differences, with 95% confidence intervals, were pooled using a random-effects model. The authors did not state that they assessed heterogeneity. The number needed to treat and the number needed to harm was calculated.

Sensitivity analysis was conducted by removing individual trials from the analysis.
Results of the review
Seven trials were included in the review (n=3,808 patients).

Compared with a regimen of multiple doses of prophylactic antibiotics, administration of a single preoperative dose did not yield a significantly reduced risk of infection. Similarly, the pooled risk difference did not significantly differ between the two treatment strategies.

Sensitivity analysis showed that the results were robust to the removal of trials from the analysis.

Authors’ conclusions
In the setting of closed long bone fractures, the pooled results failed to demonstrate superiority of multiple-dose antibiotic prophylaxis over a single-dose strategy.

CRD commentary
The review question was clear and supported by appropriate inclusion criteria. Appropriate sources were searched for literature. There were no language restrictions. Study selection was performed in duplicate to reduce the chance of error or bias, but the data extraction was undertaken by a single reviewer and may have been subject to error and bias.

Trial quality was not assessed; this made it difficult to assess the reliability of the review findings. Trials were combined using meta-analysis and, although no formal assessment of statistical heterogeneity was reported, the authors did report that confidence intervals in the forest plot overlapped, suggesting trials were sufficiently similar to justify pooling.

Given some shortcomings in the review process, the uncertain quality of included trials and variability across antibiotics and dosing schedules, the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated that no definitive recommendations could be made regarding the use of single-dose or multi-dose antibiotic regimens.

Research: The authors stated that further research is required to ensure that prophylaxis decisions are evidence based, and cost-effectiveness analysis is used to provide an insight into the optimal prophylaxis strategy.

Funding
Not stated.

Bibliographic details

PubMedID
18404036

DOI
10.1097/BOT.0b013e31816b7880

Original Paper URL
http://journals.lww.com/jorthotrauma/pages/articleviewer.aspx?year=2008&amp;issue=04000&amp;article=00010&amp;amp;type=abstract

Indexing Status
Subject indexing assigned by NLM
MeSH
Anti-Bacterial Agents /administration & dosage; Antibiotic Prophylaxis /methods; Drug Administration Schedule;
Fractures, Closed /drug therapy /surgery; Humans; Odds Ratio; Orthopedic Procedures /methods

AccessionNumber
12008104524

Date bibliographic record published
31/03/2009

Date abstract record published
01/12/2010

Record Status
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the reliability of the review and the conclusions drawn.