A systematic review and meta-analysis of antibiotic-impregnated bone cement use in primary total hip or knee arthroplasty

CRD summary
This systematic review concluded that antibiotic-impregnated bone cement could reduce the deep infection rate, in primary total joint arthroplasty, but not the superficial infection rate. The low event rates for deep infection, and the poor quality of the included trials, reduce the reliability of these conclusions.

Authors' objectives
To assess the safety and effectiveness of using antibiotic-impregnated bone cement, for primary total joint arthroplasty, to reduce the rate of surgical-site infection.

Searching
MEDLINE, EMBASE, CBMdisc and The Cochrane Library were searched in June 2013, for published studies; search terms were reported. No language or date limits were used.

Study selection
Randomised controlled trials (RCTs) that compared antibiotic-impregnated bone cement with plain bone cement or systemic antibiotic, in patients undergoing primary total hip or knee arthroplasty or both, were eligible for inclusion. Trials in which patients had a poor physical condition, for example diabetes or malignancy, were not eligible. The primary outcome of interest was the postoperative infection rate, including superficial and deep infections. Secondary outcomes included radiographic evaluation and clinical joint score.

The included trials were published between 1979 and 2013, most were in European countries, one was in Canada and one was in Taiwan. Half the trials included patients undergoing primary total hip arthroplasty, other half were of total knee arthroplasty or total hip and knee arthroplasty. The mean age of participants ranged from 63 to 75 years, where reported. The type of cement was palacos, Simplex P or CMW, and the type of antibiotic in the cement was gentamicin, tobramycin, cefuroxime, or erythromycin and colistin.

The authors did not state how many reviewers selected the studies.

Assessment of study quality
Two reviewers assessed the quality of the included trials, using a modified Jadad scale; disagreements were resolved by discussion. Trials that scored 3 or more on the Jadad scale were classified as high quality, and those scoring 2 or less were classified as low quality.

Data extraction
Two reviewers independently extracted the relative risks for dichotomous data, and mean differences for continuous data; disagreements were resolved by discussion and consultation with a third reviewer. Trial authors were contacted by email if relevant data were missing.

Methods of synthesis
Relative risks or mean differences, with 95% confidence intervals, were pooled using DerSimonian and Laird random-effects or Mantel-Haenszel fixed-effect models, depending on the presence (p<0.10; I²>50%) or absence of heterogeneity.

Subgroup assessment was undertaken by control treatment (plain bone cement or systemic antibiotic), type of surgery (hip, knee or hip and knee), and type of antibiotic. Publication bias was assessed using funnel plots.

Results of the review
Eight RCTs were included in the review (6,318 arthroplasties; range 25 to 2,948). All trials had adequate randomisation,
but concealment of allocation was unclear for six trials. Only two trials were blinded (one single and one triple). Five trials reported drop-outs; one had a very high rate (40%). Three trials scored 1 on the Jadad scale, three scored 2, one scored 3, and one scored 4; six trials were classified as low quality. Follow-up ranged from three to 49 months; in most trials it was 24 months or more. The funnel plot for the analysis of deep infection rate displayed mild asymmetry.

Seven trials reported the rate of deep infection and five reported the rate of superficial infection.

The deep infection rate was statistically significantly lower with antibiotic-impregnated bone cement than without it (RR 0.41, 95% CI 0.17 to 0.97; I²=53%; seven RCTs). In the subgroup analysis, the deep infection rate was statistically significantly lower with antibiotic-impregnated bone cement, compared with systemic antibiotic (RR 0.37, 95% CI 0.14 to 0.98; I²=0; three RCTs). The difference was not statistically significant between antibiotic-impregnated bone cement and plain bone cement (four RCTs).

The superficial infection rate was statistically significantly higher with antibiotic-impregnated bone cement than without it (RR 1.47, 95% CI 1.13 to 1.91; I²=0; five RCTs). In the subgroup analyses, the superficial infection rate was statistically significantly higher with antibiotic-impregnated bone cement, compared with systemic antibiotic (RR 1.48, 95% CI 1.10 to 2.00; three RCTs). The difference was not statistically significant between antibiotic-impregnated bone cement and plain bone cement (two RCTs).

Further subgroup results were presented, along with a narrative synthesis of the results for secondary outcomes.

**Authors' conclusions**

Antibiotic-impregnated bone cement could reduce the deep infection rate, in primary total joint arthroplasty, but not the superficial infection rate.

**CRD commentary**

The review question and inclusion criteria were clear. Appropriate sources were searched for relevant trials, but only published studies were sought; the funnel plot suggested minimal publication bias. No language restrictions were applied, reducing the potential for language bias. Two reviewers independently extracted the data and assessed validity, reducing the potential for reviewer error and bias. It was unclear how many reviewers selected the trials. Trial validity was assessed using a simple tool, with only basic information reported, but it was apparent that most of the included trials were of low quality, reducing the reliability of their results. The synthesis appears to have been appropriate.

The authors acknowledged the uncertain quality of the included trials, and their different interventions and patient populations, with exposure to different types of bacteria, according to the location of the trial. This was a reasonably good systematic review, but the low event rates for deep infection, and low or uncertain quality of most of the trials, reduces the reliability of the conclusions.

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

**Practice:** The authors stated that without the full adverse-effect profile of systemic antibiotic use, local delivery by antibiotic-impregnated bone cement could solve the problem of deep prosthetic infection.

**Research:** The authors stated that more sufficiently powered trials were required to evaluate the efficacy and safety of antibiotic-impregnated bone cement for primary total joint arthroplasty. Research should assess other adverse effects, such as antibiotic resistance, allergic reaction, and toxicity, and the cost.

**Funding**

No funding received.

**Bibliographic details**


**PubMedID**

24349353
DOI
10.1371/journal.pone.0082745

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Bacterial Agents /administration & dosage; Antibiotic Prophylaxis; Arthroplasty, Replacement, Hip /adverse effects; Arthroplasty, Replacement, Knee /adverse effects; Bone Cements; Humans; Incidence; Odds Ratio; Postoperative Complications /prevention & control; Prosthesis-Related Infections /prevention & control; Publication Bias

AccessionNumber
12014000236

Date bibliographic record published
13/01/2014

Date abstract record published
03/09/2014

Record Status
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.