Antibiotics and antiseptics to prevent infection in cardiac rhythm management device implantation surgery
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CRD summary
This review concluded that perioperative intravenous antibiotic prophylaxis, within one hour before cardiac electronic device implantation, effectively reduced surgical site infections. Compared to perioperative use, postoperative antibiotics resulted in statistically significantly higher infection rates. As data came from studies of poor or questionable quality, and limited data was available for individual comparisons, conclusions should be treated with caution.

Authors' objectives
To assess whether the prophylactic use of antibiotics and antiseptics, in patients undergoing cardiac implantable electronic device implantation, reduced the incidence of surgical site infections.

Searching
MEDLINE (including in-process and non-indexed citations), EMBASE and CINAHL were searched to April 2011. The Cochrane Wounds Group Specialized Register and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to February 2012. Search terms were reported in an appendix obtained from authors. No date or language restrictions were applied. Five relevant journals and bibliographies of identified studies were checked. Corresponding authors and manufacturers were contacted. The US Food and Drug Administration briefing documents were checked.

Study selection
Randomised controlled trials (RCTs) that assessed the effects of antibiotic prophylaxis and antiseptics on longer or short term rates of surgical site infection were eligible for inclusion. Patients had to be undergoing cardiac implantable electronic device implantation. Studies on initial or repeat implantation of pacemaker or cardioverter-defibrillator were included. All participants were assumed to have had perioperative antiseptics. Eligible antibiotic regimes included perioperative systemic administration (intravenous or oral), or local administration to surgical site. Comparators included local antiseptic alone, no antibiotics or placebo and comparisons between different antibiotics and/or administration regimes. The primary outcomes of interest were rates of infections (including septicaemia, endocarditis, unspecified valve infection, cellulitis) and acute adverse events.

In the studies, systemic antibiotics used included (separately or in combination) cephalothin, cefazolin, cefazadone, cefamandole, cefoxitin, cefotaxime, cefuroxime, flucloxacillin, cloxacillin, mezlocillin, ampicillin, cloxacillin, teicoplanin, vancomycin and levofloxacin. Local antibiotics included rifampicin, cloxacillin, gentamicin and combination of neomycin, bacitracin and polymyxin. In most studies systemic antibiotics were administered at one hour or less before procedure, but in some studies it was two hours before, or timing was unclear. Cessation of antibiotics varied from immediately post procedure to seven days. Where reported, the antiseptics used included chlorhexidine, povidone-iodine and chlorhexidine, or povidone-iodine and a combination of Savlon, ether and iodine. In one study antibiotics plus local antiseptic infiltration to wound was compared to antibiotics alone.

Two reviewers assessed studies for inclusion. Disagreements were resolved by discussion or a third reviewer.

Assessment of study quality
Quality was assessed using the Cochrane Collaboration risk of bias tool. This was based on sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting and other issues. A risk of bias table summarised outcomes.

Two reviewers independently assessed study quality. Disagreements were resolved by discussion and consensus.

Data extraction
Data were extracted in order to calculate risk ratio and 95% confidence intervals.
One reviewer extracted data, and a second reviewer checked it. Where necessary, authors were contacted for missing information.

**Methods of synthesis**
Where studies were considered clinically similar, and statistical heterogeneity was low ($I^2$ less than 40%) pooled risk ratio and 95% confidence intervals were calculated using a fixed-effect model. Heterogeneity was assessed using $I^2$. Subgroup analyses investigated different antibiotic regimes (timing, and methods of delivery). Effects of type of procedure (primary or repeat) were also investigated (method unclear). Publication bias was assessed using funnel plots.

**Results of the review**
Fifteen RCTs (3,970 participants) were included. Dates of publication ranged from 1978 to 2009. Follow-up ranged from one week or less to 43 months.

The quality of studies was generally poor to moderate. In particular sequence generation, and allocation concealment was unclear in all studies, and in most studies blinding was unclear or not undertaken.

Compared to no antibiotics, intravenous antibiotics reduced the risk of infection (RR 0.13, 95% CI 0.05 to 0.36; $I^2=0$%; six RCTs). One trial (100 participants) reported on adverse events, with three events reported in the antibiotic group and none in the control group. There was no statistically significant difference between primary and repeat procedures (six studies; $I^2=39$%).

There was no statistically significant difference in risk of infection between intravenous and local antibiotics ($I^2=0$%; two RCTs). Two RCTs compared the timing of intravenous antibiotics: in one perioperative intravenous antibiotics were statistically significantly better than postoperative antibiotics; results for the second were not reported.

Other comparisons were available in single studies only. None showed statistically significant results.

**Cost information**
Health care costs, as reported in RCTs, were sought but no evidence was identified.

**Authors’ conclusions**
Perioperative intravenous antibiotic prophylaxis within one hour before cardiac electronic device implantation effectively reduced site infections. Compared to perioperative use, postoperative antibiotics resulted in statistically significantly higher infection rates.

**CRD commentary**
The aims of the review were clearly stated in terms of inclusion criteria. The search included looking for studies in any language and for unpublished studies. This was likely to have reduced potential language or publication bias. Methods of the review aimed to reduce possible reviewer error or bias. Quality was assessed and methods of synthesis appeared generally appropriate; the method of assessing differences in outcomes between primary and follow up procedures wasn’t clear, but appeared to be based on pooling data from the treatment groups only. Details of included studies were limited, in particular regarding the participants.

Data came from studies of poor or questionable quality, and limited data was available for individual comparisons so conclusions should be treated with caution.

**Implications of the review for practice and research**
**Practice:** The authors stated that perioperative antibiotic prophylaxis for cardiac electronic device implantation should be part of a comprehensive surgical-site infection program administered at any hospital.

**Research:** The authors stated that further well designed RCTs were needed to assess the effects of antibiotics, and local antiseptic infiltration, in people undergoing cardiac device implantation. Follow-up should be longer than one year to take account of possible effects of biofilm development on infection rate. Outcomes should include costs.

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