A meta-analysis of hemodialysis catheter locking solutions in the prevention of catheter-related infection

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CRD summary
The review concluded that antibiotic locking solutions reduced the frequency of catheter-related infections without significant side-effects. The authors' conclusions reflected the evidence presented, but the extent to which the findings were generalisable was unclear due to limited exploration of clinical variation and statistical heterogeneity in the main analysis.

Authors' objectives
To assess the efficacy of antimicrobial locking solutions in decreasing catheter-related infection rates.

Searching
MEDLINE, EMBASE, CINAHL and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for published studies in English up to 2007. Search terms were reported. Reference lists of retrieved papers were reviewed. Four major renal journals were reviewed. Four databases of ongoing controlled trials and the grey literature were searched for unpublished studies.

Study selection
Randomised controlled trials (RCTs) of adult patients (aged >18 years) who received haemodialysis through a central or venous catheter and used one or more antimicrobial locking solutions as the intervention and heparin lock solution as control were eligible for inclusion. Studies that assessed either tunneled or non-tunneled catheters were eligible for inclusion. RCTs that examined antimicrobial impregnated tubing or exit-site cleaning solutions alone were excluded. Studies in which catheters were not used solely for haemodialysis were excluded.

Both incident (starting dialysis) and prevalent acute renal failure and chronic end-of-stage renal disease patients were included. Catheter variables of interest included duration in situ, position site and catheter brand. The primary outcome was catheter-related infection per 1,000 catheter days patients who used antimicrobial locking solutions and those who used heparin only. Secondary outcomes were rates of catheter dysfunction, bleeding, mortality and effects on haemoglobin level. Adverse events were assessed.

Four trials included tunneled catheters only, one trial included non-tunneled catheters only and two trials included a mixture of the two catheters. All except one of the trials recruited both incident and prevalent haemodialysis patients. Six trials used heparin 5,000U/mL as control. Antibiotics assessed included gentamicin, cefotaxime, minocycline and cefazolin/gentamicin combination. Non-antibiotic solutions assessed were taurolidine and high concentration of citrate (30%).

One reviewer screened titles and abstracts and two reviewers independently screened the full papers.

Assessment of study quality
Two reviewers independently assessed quality of the included trials on methods of randomisation and blinding. The number of participants lost to follow-up in each trial was reported. Disagreements were resolved by discussion.

Data extraction
Primary and secondary outcomes data were extracted for calculating rate ratios (RRs) with 95% confidence intervals (CIs).

It was unclear how many reviewers extracted data.
Methods of synthesis
Rate ratios with 95% CIs were combined in a meta-analysis using a random-effects model with generic inverse variance component. Cells with zero counts were replaced with a factor of 0.5.

Heterogeneity between trials was assessed by $\chi^2$ and $I^2$ statistics. Subgroup analysis was conducted for gentamicin (the one antibiotic assessed in more than one trial) based on high and low doses.

Results of the review
Seven RCTs (n=624 patients) met the inclusion criteria. Three trials were described as double-blind and four were single-blind.

Catheter-related infection was 7.72 times lower with antimicrobial locking solutions compared with heparin locks (95% CI 5.1 to 10.3; seven trials, n=624 patients). Using absolute risk reduction, this translated to a number needed to treat (NNT) of three to prevent one catheter-related infection per 100 catheter-days. Catheter-related infection rates in heparin groups were similar across all studies (range 2.1 to 4.1 per 1,000 catheter-days). Catheter-related infection rates achieved with the different antimicrobial locking solutions were of similar magnitude. Statistical heterogeneity was not reported.

Gentamicin showed to be an effective antimicrobial locking solution in a pooling of both high and low doses of the drug (RR 11.8, 95 CI 8.4 to 15.3; three studies), but heterogeneity was high ($I^2=81.6\%$).

Only single studies were available for other antimicrobial locking solutions. There was significantly lower mortality from catheter-related infection in patients who used antimicrobial locking solutions (two studies). Of the five studies assessing exit-site infections, two found fewer infections in the antimicrobial locking solutions arm, two reported no difference between the antimicrobial locking solutions group and heparin group and one study observed no exit-site infection during the study.

Generally, rates of adverse events were low across the studies and rates of catheter thrombosis did not increase with antimicrobial locking solutions.

Authors' conclusions
The review confirmed that antibiotic locking solutions reduced the frequency of catheter-related infection without significant side-effects.

CRD commentary
This review addressed a well-defined question in terms of participants, interventions, outcomes and study design. The search included appropriate electronic databases, but the restriction to English-language studies meant that language bias could not be ruled out. Two reviewers independently selected studies and assessed trial quality. It is unclear how many reviewers extracted data, so errors and bias could not be ruled out. Characteristics of the individual trials were presented. The assessment of quality of the included studies was appropriate, but was not taken into account in the synthesis and conclusions. Heterogeneity was assessed, but not reported for the main analysis. The authors highlighted that it was not possible to definitively assess risks of development of antibiotic resistance due to the short duration of follow-up.

The authors' conclusions reflected the evidence presented, but the extent to which the findings were generalisable was unclear due to limited exploration of clinical variation and statistical heterogeneity in the main analysis.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that longer follow-up was necessary to evaluate development antibiotic resistance.
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