Prevention of bloodstream infections with central venous catheters treated with anti-infective agents depends on catheter type and insertion time: evidence from a meta-analysis

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Authors' objectives
To determine the effect of anti-infective coating or cuffing of central venous catheters (CVC) on the risk of catheter-related infection.

Searching
MEDLINE (to January 2000), EMBASE (to January 2000) and the Cochrane Library (Issue 1, 2000) were searched for studies published in full, in peer-reviewed journals in any language. Reference lists were also checked. Data presented in abstracts, letters or reviews were excluded.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. Studies in which the patients were allocated by date of birth, hospital number and alternate allocation were included. Trials that did not have a random or quasi-randomly allocated control group were excluded. Most of the included studies were not blinded.

Specific interventions included in the review
Studies that compared any antiseptic or antimicrobial-coated cuffed CVC with a similar uncoated or uncuffed catheter were eligible for inclusion. Only studies of catheters inserted percutaneously were included. Studies of catheters being exchanged over a guidewire were excluded. The included studies were of anti-infective catheters treated with chlorhexidine-silver sulfadiazine coating, silver-impregnated collagen cuffing, antibiotic coating (teicoplanin, minocycline plus rifampin, vancomycin, and cefazolin) or silver coating. In the included studies, the average catheter insertion time varied between 2 and 147 days. Most catheters had three lumens.

Participants included in the review
Studies of adults were eligible for inclusion. The included studies were of intensive care patients, oncologic patients, surgical patients, patients receiving total parenteral nutrition, or mixed populations.

Outcomes assessed in the review
Studies that reported either catheter colonisation per 100 catheters or bloodstream infection (BSI) per 100 catheters were eligible for inclusion. The studies had to report data in dichotomous form according to definitions used by the original authors. Catheter colonisation was defined as the documented growth from a proximal or distal catheter segment of either 15 or more colony-forming units (CFU) in a semi-quantitative culture, or more than 1,000 CFU in a quantitative culture. Cultures were obtained from the external surface only, or from both the internal and the external surfaces of the catheters. BSI was defined as the isolation of the same organism from (semi)quantitative culture of a catheter segment and from the patient's blood in the absence of another source of infection. The primary outcome in the review was BSI. Adverse events were also assessed. The mean duration of observation ranged from 2 to 147 days.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Validity was assessed using the Jadad scale, which scores randomisation method, blinding and drop-outs (see Other Publications of Related Interest). Three reviewers independently assessed validity and reached consensus through discussion.
Data extraction
One reviewer extracted the data and two others independently checked the data extracted. For each study, the numbers of catheters in the treatment and control groups that became colonised and the numbers of BSI per catheter inserted were extracted. Average catheter insertion times were also extracted.

Methods of synthesis
How were the studies combined?
The trials were combined using a meta-analysis when the authors considered them to be clinically homogeneous. The pooled relative risk (RR) and 95% confidence interval (CI) were calculated for colonisation using a fixed-effect model. The odds ratio (OR) and 95% CI for BSI were calculated using the Peto model. This was done separately for antibiotic-coated, silver-impregnated collagen cuffed, and chlorhexidine-silver sulfadiazine-coated catheters.

How were differences between studies investigated?
The incidence of event rates (colonisation and BSI separately) for anti-infective catheters was plotted against the incidence for control catheters.

Statistical heterogeneity in the meta-analysis was tested using the chi-squared statistic. A sensitivity analysis was performed to assess the influence of the average duration of catheterisation on the rates of BSI for different types of catheters.

Results of the review
Twenty-three trials (4,660 catheters) were included. There were 18 RCTs (3,562 catheters) and 6 studies that used quasi-randomised methods (1,098 catheters).

Quality: 7 of the 18 RCTs scored three or more points out of five; the 6 quasi-randomised trials scored only one point. This suggests that most of the included studies were of poor quality.

Catheter colonisation (22 trials): the meta-analysis showed that anti-infective catheters significantly reduced colonisation (RR 0.61, 95% CI: 0.51, 0.72). However, significant heterogeneity was detected (P<0.001).

BSI (18 trials): the meta-analysis showed that anti-infective catheters significantly reduced BSI (OR 0.63, 95% CI: 0.45, 0.87). No significant heterogeneity was detected (P=0.329)

Impact of insertion time (15 trials, 16 comparisons). Antibiotic-coated catheters significantly reduced BSI in 2 trials (343 CVCs) with a mean insertion duration of 6 days; the pooled OR was 0.14 (95% CI: 0.04, 0.51). No trials had longer insertion times. There was no significant difference in BSI between silver-impregnated collagen cuff catheters and control catheters in 3 trials (422 CVCs) with an average insertion time of 5 to 8.2 days (OR 0.54, 95% CI: 0.21, 1.36). A fourth trial (101 CVCs) found no significant difference between silver-impregnated collagen cuff catheters and control catheters after an average insertion time of 38 days (OR 1.15, 95% CI: 0.16, 8.49). Pooling data from the 2 RCTs with the longest insertion times found no significant difference.

Chlorhexidine-silver sulfadiazine coated catheters significantly reduced BSI in 5 trials (1,269 CVCs) with an average insertion duration of 5.2 to 7.5 days; the pooled OR was 0.48 (95% CI: 0.25, 0.91). There was no significant difference in BSI between chlorhexidine-silver sulfadiazine-coated catheters and uncoated catheters in 5 trials (1,544 CVCs) with an average insertion duration of 7.8 to 20 days (pooled OR 0.94, 95% CI: 0.58, 1.54).

Adverse events (12 trials): one trial found that cuffed catheters were more difficult to insert than control catheters, while three other trials (including 1 RCT) found that cuffed catheters were more easily extruded than control catheters. None of the trials reported any cases of systemic allergic reactions or local hypersensitivity.

Cost information
The authors stated that anti-infective catheters cost about twice as much as conventional catheters.
Authors' conclusions
Antibiotic and chlorhexidine-silver sulfadiazine-coated catheters reduce infections when they are inserted for short periods (less than 1 week). For longer insertion times, no studies were identified on the use of antibiotic-coated catheters and there was evidence of no benefit for chlorhexidine-silver sulfadiazine-coated catheters. There was also evidence of no benefit for silver-impregnated collagen cuff catheters in either the long- or the short-term.

CRD commentary
The review question was clear in terms of the study design, intervention, participants and outcomes. Several relevant sources were searched, the search terms were stated, and no language limitations were applied. No attempt was made to locate unpublished studies, thus raising the possibility of publication bias. The methods used to select the studies were not described; hence, it is not known whether efforts were made to reduce selection bias. More than one reviewer independently assessed validity, while the data extraction was performed by one reviewer and checked by another two; this reduced the potential for bias and errors. The validity of the RCTs and quasi-randomised studies was assessed using criteria validated for the reporting of RCTs. The data from randomised and quasi-randomised trials were pooled, but study quality was not taken into account in the analysis or the conclusions. Poor-quality studies tend to overestimate treatment effects. There was insufficient information about the number of patients and the unit of randomisation (patient or catheter) in the individual studies to be sure that the unit of analysis (catheters) used in the meta-analysis was appropriate. If it was not and no adjustments were made, the analysis might have overestimated the effectiveness of anti-infective CVCs. The finding of significant heterogeneity for catheter colonisation rates suggests that a meta-analysis may not have been appropriate for this outcome. Having found significant heterogeneity for colonisation rate, the authors did not explore potential reasons for this. These concerns indicated that the findings of the review may not be reliable.

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

Research: The authors stated that further research is required to assess the optimal type of CVC and the optimal time at which to replace CVCs, and to identify which patients would benefit most from anti-infective CVCs. They also stated that the cost-effectiveness of anti-infective CVCs needs to be assessed.

Bibliographic details
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Other publications of related interest

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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.