Effectiveness of impregnated central venous catheters for catheter related blood stream infection: a systematic review

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CRD summary
This review assessed whether impregnated CVCs provide any advantage over standard CVCs in terms of CR-BSI or catheter colonisation. It concludes that heparin-coated or antibiotic-impregnated CVCs provide the optimal approach but that further research is needed to determine which is superior. The authors’ conclusions may be overly strong given the study numbers and quality, especially regarding heparin-coated CVCs.

Authors' objectives
To examine the effectiveness of four different types of impregnated or coated central venous catheters (CVCs) for the reduction of catheter-related blood stream infection.

Searching
The reference lists of existing reviews of the effectiveness of impregnated CVCs were screened for relevant studies. Electronic searches of the PubMed, TRIP and Cochrane Central Register of Controlled Trials databases were conducted to identify studies published in the previous two years (years not provided). The search terms are stated to be available from the authors. No language restrictions were reported.

Study selection
Randomized or quasi-randomized controlled trials comparing the effect of any one of four types of impregnated CVC either against standard CVCs or against each other. CVCs could be impregnated or coated with heparin chlorhexidine plus silver sulphadiazine (CH-SS), antibiotics or silver.

The majority of included trials used polyurethane CVCs (mean duration five to 22 days) except for two trials of silicone CVCs (mean duration 29 to 66 days). The majority of included patents were adults admitted to intensive care units, although haematology, burns, oncology or bone-marrow transplant patients were also included. One trial was limited to paediatric intensive care. One trial with patients undergoing haemodialysis was excluded. Outcomes of interest were catheter-related blood stream infection (CR-BSI) or catheter colonisation. The criteria for diagnosing CR-BSI were reported to be similar across studies.

The authors did not state how papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Study quality was assessed against three criteria: concealment of randomisation, clinician blinding to the type of CVC and the percentage of patients randomised who had outcomes reported CR-BSI.

The authors did not state how validity assessment was performed.

Data extraction
Data were extracted on number of patients with CR-BSIs and number with catheter colonisation.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
A random effects model was used to combine studies due to variation in the patient population and baseline risk of CR-BSI across studies. Statistical heterogeneity was assessed using the $\chi^2$ test. The $I^2$ test for heterogeneity was also
Results of the review

Thirty-seven trials reporting 41 CVC comparisons (11,586 patients) were included. Concealment of allocation was reported as adequate for 14 trials and not adequate for six. Clinicians were reported to be blinded to allocation for 10 trials and not blinded for 20 trials. Seven trials reported both adequate concealment of randomisation and blinding of clinicians. The rate of follow-up ranged from 71% to 100%.

For the outcome CR-BSI, heparin bonded CVCs reduced the risk of infection by 84% (RR 0.16, 95%CI: 0.06, 0.43, \( \chi^2 P = 0.42 \)), based on three trials (n=462), none of which reported both adequate randomisation and blinding. Antibiotic impregnated CVCs reduced the risk by 72% (RR 0.28, 95%CI: 0.15, 0.54, \( \chi^2 P = 0.65 \)), based on seven trials (n=1747), three with adequate randomisation and blinding. The comparisons of CH-SS impregnated and silver-impregnated CVCs against standard CVCs showed a trend towards lower rates of infection in the impregnated CVC groups, but neither comparison reached statistical significance.

The only head-to-head comparison of impregnated CVCs to reach statistical significance was that for antibiotic impregnated against CH-SS impregnated CVCs, with lower rates of infection in the antibiotic impregnated group (RR 0.12, 95%CI: 0.02, 0.670, \( \chi^2 P = 0.48 \)). This was based on two trials (n=812), one with adequate randomisation and blinding.

In terms of catheter colonisation, one small RCT showed a statistically significant benefit from heparin CVCs compared to standard CVCs (RR 0.42, 95%CI: 0.18, 0.99, n=32). CH-SS impregnated CVCs reduced the risk of colonisation by 42%, however the 16 trials (n=3,939) were found to be highly heterogeneous (RR 0.58, 95%CI: 0.43, 0.77, \( \chi^2 P<0.001 \)). Only two of the 16 trials reported adequate randomisation and blinding. The six trials (n=1,357) comparing antibiotic impregnated CVCs against standard, found a 62% reduction in colonisation from antibiotic impregnation, however the studies were again highly heterogeneous (RR 0.38, 95%CI: 0.21, 0.71, \( \chi^2 P=0.0005 \)).

For the head-to-head comparisons of impregnated catheters, antibiotic impregnated CVCs were found to be significantly more effective than both silver impregnated (one trial) and CH-SS impregnated (two trials) catheters. CH-SS impregnated CVCs were also shown to be more effective at reducing catheter colonisation than heparin impregnated catheters (one trial).

Cost information

Antibiotic-impregnated and heparin-coated CVCs were reported as being almost double the price of standard CVCs in the UK, with CH-SS catheters slightly cheaper.

Authors' conclusions

Heparin-coated or antibiotic-impregnated CVCs provide the best means of reducing catheter-related blood stream infection.

CRD commentary

The review aim and inclusion criteria are clear and well set out. The decision to include lower quality quasi-randomised studies was not justified and may be questioned given the volume of evidence available. The literature search relied predominantly on references from existing reviews, with no indication whether these were systematic reviews that had themselves used comprehensive search strategies. This source was supplemented with electronic searches covering the preceding two years but, as the search years were not given, it was not possible to determine how recently the searches were undertaken. No language restrictions were reported and no attempt was made to identify unpublished literature, leaving open the possibly of language and publication bias. The methods used to undertake the review were not reported, giving rise to potential selection bias and/or reviewer bias. Important methodologic features, concealment of allocation and clinician blinding, were assessed; however details regarding what was considered adequate/inadequate were not provided. An appropriate random-effects meta-analysis was carried out but no attempt to investigate potential sources of heterogeneity was conducted, even where statistical heterogeneity was identified. Given the inclusion of quasi-randomised trials and the poor reporting of both randomisation and blinding, some sensitivity analysis would have been informative. The authors' conclusions are in part too strong for the evidence reported. In particular, the evidence
for heparin-coated CVCs comes from only a few relatively small RCTs, one of which reports the heparin CVCs to have poorer outcomes compared to CH-SS-impregnated CVCs. The evidence presented for antibiotic-impregnated CVCs is more convincing and their superiority over CH-SS CVCs has been confirmed by one large high quality trial. Although the authors acknowledge the poor quality of many of the studies, they do not point out the implications of this for their conclusions.

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

Research: The authors stated that a large well designed randomised controlled trial is required to determine whether heparin-coated or antibiotic-impregnated CVCs are the most effective. Simpler and more clinically relevant outcome measures focusing on blood stream infections that require treatment should be used. Other clinically relevant outcomes include duration of hospital or ICU stay and mortality.

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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.