Anti-infective-treated central venous catheters for total parenteral nutrition or chemotherapy: a systematic review

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CRD summary
This review assessed the use of anti-infective-treated central venous catheters in patients requiring a central venous catheter for total parenteral nutrition or chemotherapy and concluded that there was insufficient evidence to recommend their use. The review was generally well conducted. It identified potentially significant sources of bias in the selected trials.

Authors' objectives
To assess the effects of anti-infective central venous catheters (CVCs) on catheter-related bloodstream infection (CRBSI) in patients who received a CVC for total parenteral nutrition (TPN) or chemotherapy.

Searching
MEDLINE and the Cochrane Library were searched from inception to 14 October 2007. Search terms were reported. Reference lists of all identified trials were searched. No language restrictions were applied.

Study selection
Studies eligible for inclusion were: randomised and quasi-randomised controlled trials (RCTs) or systematic reviews of these study designs that compared anti-infective (antiseptic or antibiotic treated) CVCs with standard CVCs in patients undergoing chemotherapy or TPN that supplied a definition of CRBSI. The outcome of interest was the incidence of CRBSI. Included studies most commonly used a CVC inserted in the subclavian or jugular vein and treated with chlorhexidine-silver sulfadiazine. The mean duration of catheterisation ranged from 10 to 66 days.

Two reviewers independently assessed the studies for inclusion in the review. Disagreements were resolved by discussion.

Assessment of study quality
Validity was assessed on the basis of adequacy of randomisation and blinding, description of drop-outs and analysis by intention to treat.

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Data extraction
Data on duration of CVC placement and the incidence of CRBSI were extracted and baseline incidence density, incidence density ratio (IDR) and incidence density difference (IDD) were calculated.

Data extraction was performed by two reviewers independently and cross-checked. If necessary, additional information was requested from the original investigators.

Methods of synthesis
The pooled IDDs or IDR s and corresponding 95% confidence intervals (CIs) were calculated using a random-effect meta-analysis. The number of catheterisation days needed to treat (NNT) were calculated from the pooled IDDs. Sub-group analyses were carried out where applicable. These were not defined a priori. Statistical heterogeneity was assessed using the $X^2$ and $I^2$ test. Publication bias was examined using a funnel plot.

Results of the review
Nine RCTs were included in the review (n=2,202).
Quality
The authors remarked that in general the quality of included studies was low. Six trials had unclear or inadequate allocation concealment and six gave an inadequate description of drop-out rates. Analysis by intention to treat was not performed in six of the trials and was unclear in the remaining three. Only one RCT was described as double blind.

Antibiotic-treated CVCs versus standard CVCs (one RCT, n=356)
This trial found that antibiotic-treated CVCs reduced the occurrence of CRBSI in outpatients receiving chemotherapy IDR -1.03 (95%CI -1.76, -0.3; p=0.005). The mean insertion time to avoid one case of CRBSI was estimated to be 63 days.

Antiseptic-treated CVCs versus standard CVCs (eight RCTs, n=1,846)
There was no significant benefit of using antiseptic-treated CVCs. The mean insertion time to avoid one case of CRBSI was estimated to be 14.6 days. Significant heterogeneity was not detected using $\chi^2$. The only subgroup analysis to demonstrate a significant benefit of antiseptic-treated CVCs was in patients with a relatively high incidence of CRBSI, IDR 0.44 (95% CI 0.20, 0.93; p=0.03).

The regression curve for the NNT as a function of baseline incidence density did not establish a relationship between the treatment effect and the underlying risk.

Publication bias was not detected by a funnel plot.

Authors' conclusions
There was insufficient evidence to recommend anti-infective-treated CVCs in patients receiving chemotherapy or TPN.

CRD commentary
The review addressed clear research questions. Inclusion criteria appeared to be appropriate, although the relatively short-term catheter placement in the antiseptic-treated CVC group raised the question of whether the patients involved in the trials were representative of patients receiving CVCs for TPN or chemotherapy in the general population. Two relevant sources were searched and attempts were made to limit language bias. There was no apparent attempt to locate unpublished material, which meant that relevant studies may have been missed. Publication bias was not detected by funnel plot, but could not be ruled out completely. Methods were used to minimise reviewer error and bias in the selection of studies and data extraction. Validity was assessed systematically and revealed concerns about the potential risk of bias in the selected studies. Methods of analysis were appropriate, but the results of the sub-group analyses should be regarded with particular caution as these were not defined a priori. The authors stated that almost all the included studies were supported by industry. In the light of the potential limitations highlighted, the authors' cautious conclusions were appropriate.

Implications of the review for practice and research
Practice: The authors stated that anti-infective-treated CVCs should be considered when background rates of CRBSI remain high despite good hygienic practice, but should be limited to patients expected to require CVCs for a maximum period of 10 days.

Research: The authors stated that there was a need for large high-quality RCTs to assess the preventive benefit of anti-infective CVCs in patients receiving a CVC for TPN or chemotherapy. Patients with a high baseline incidence density despite good hygiene practices should be included, and CVCs treated internally and externally investigated. Specific measures of CRBSI should be used and information necessary to calculate the risk per 1,000 catheter days should be reported.

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