Central venous catheters treated with anti-infective agents in preventing bloodstream infections

The clinical effectiveness and cost-effectiveness of central venous catheters treated with anti-infective agents in preventing bloodstream infections: a systematic review and economic evaluation

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Executive summary

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Executive summary

Background

Central venous catheters (CVCs) include a variety of vascular access devices with a wide range of clinical applications. Although CVCs have had a profound impact on the range and quality of care offered to patients in both hospital and domiciliary settings, their use is also associated with a variety of complications, most notably infection. Such infections may develop in the soft tissues, or be introduced directly through the lumen of the CVC into the bloodstream. The morbidity and mortality associated with these infections have an impact on both the patient and the healthcare system.

Previous reviews have indicated that there may be a clinical benefit of using anti-infective central venous catheters (AI-CVCs) to reduce the complication of catheter-related bloodstream infection (CRBSI). New trial data are available and this review was conducted to integrate these data.

Objectives

The objectives of this report were to assess the clinical effectiveness and cost-effectiveness of CVCs treated with anti-infective agents in preventing CRBSIs.

Methods

The assessment was carried out according to accepted procedures for conducting and reporting systematic reviews and economic evaluations, including identification of clinical and economic studies, application of inclusion criteria, quality assessment of included studies, and data extraction and analysis.

Searching

Evidence on clinical effects and cost-effectiveness of AI-CVCs was identified using a comprehensive search strategy of bibliographic databases (including the Cochrane Library, EMBASE and MEDLINE), as well as checking of reference lists in identified studies. The database searches covered the period from 1985 to August 2005.

Inclusion criteria

The assessment was restricted to published papers of randomised controlled trials testing the clinical effectiveness of AI-CVCs. The relevant comparators were untreated CVCs or other treated catheters.

Clinical outcomes had to include at least a measure of CRBSI, colonisation or clinical signs and symptoms of CRBSI.

Economic evaluation

Only full economic evaluations (synthesis of costs and benefits) comparing the use of AI-CVCs with untreated CVCs or other treated catheters were selected for inclusion in the review.

As part of the study, the economic performance (cost-effectiveness and potential cost-savings) of using AI-CVCs to reduce the number of CRBSIs in patients requiring a CVC was estimated. A basic decision-analytic model was constructed to explore a range of possible scenarios for the NHS in England and Wales.

Results

Clinical review findings

A total of 32 trials met the clinical inclusion criteria. Owing to the diversity of definitions of CRBSI and colonisation, an outcome categorisation system was developed to differentiate among the various microbiological methods and criteria used in the different definitions.

Seven different types of AI-CVC were identified, with the most frequently tested being chlorhexidine and silver sulfadiazine (CHSS) (externally treated), CHSS (externally and internally treated) and minocycline rifampicin (internally and externally treated).

In general, the trials were of a poor quality in terms of reported methodology (e.g. method of randomisation and blinding), microbiological relevance (reporting of colonisation and not CRBSI) and control of confounding variables (patient characteristics).

▶

The pooled result suggests a statistically significant advantage for AI-CVCs in comparison to standard catheters in reducing CRBSI [odds ratio (OR) 0.45, 95% confidence interval (CI) 0.34 to 0.60, 24 studies, I^2 = 0%, fixed effects].

Analysis by subgroups of catheters demonstrates that antibiotic-treated catheters and catheters treated internally and externally decrease CRBSI rates significantly (OR 0.26, 95% CI 0.15 to 0.46, six studies, I^2 = 0%, fixed effects, and OR 0.43, 95% CI 0.26 to 0.70, nine studies, I^2 = 0%, fixed effects, respectively). Catheters treated only externally demonstrate a wider confidence interval and non-significant effect (OR 0.67, 95% CI 0.43 to 1.06, nine studies, I^2 = 0%, fixed effects).

When the duration of insertion was investigated, an average duration of between 13 and 20 days did not result in a statistically significant treatment effect. However, for trials with an average duration of between 5 and 12 days, and for the one study that had a mean duration of more than 20 days, there was a statistically significant treatment effect.

The overall treatment effect was observed for both femoral and jugular insertion sites and for those studies reporting a mix of insertion sites. The treatment effect was not observed in trials using exclusively subclavian insertion sites.

The non-significant findings related to duration and site need to be viewed with caution as the results may be more closely related to overall rates of infection or the type of AI-CVC.

Four trials compared treated catheters. One of these reported a benefit of antibiotic-treated catheters over catheters treated externally with CHSS.

Three sensitivity analyses testing for study design differences were also conducted: analysis by person or catheter, blinding and randomisation. All reported a statistically significant treatment effect.

The review is limited owing to the quality of the trials included, marked differences in the definitions and methods of diagnosis of CRBSI, and inconsistent reporting of risk factors and patient population factors. Furthermore, two-thirds of trials were commercially funded. Such limitations mean that local decisions as to whether or not to adopt AI-CVCs for the prevention of CRBSIs require a clear understanding of the evidence-based reviews and guideline recommendations as well as knowledge of local clinical practice and infection rates.

Economic review findings

Four economic evaluations met inclusion criteria for the review. Three articles were full papers; one was published as a letter. Overall, the quality of the three full economic evaluation papers was high. All of the authors adequately described the research question and comprehensively described the relevant comparators. Only two papers provided the reader with enough information to recalculate and therefore verify the size of the incremental cost-effectiveness ratios (ICERs). The authors all agree that, from a health service perspective, the use of CVCs to prevent CRBSIs is a cost-effective option compared with the use of standard CVCs when used in high-risk populations, and that use of these novel technologies leads to better patient outcomes and reduced costs.

The results from 16 partial economics evaluations are presented. These papers investigated a range of measures to reduce bloodstream infections and CRBSIs and reported associated cost-savings. All but one of the studies explicitly agrees that there are substantial monetary savings to be generated from successfully reducing the number of bloodstream infections. As partial analyses, these papers did not meet the inclusion criteria for the review, but data were used to inform the decision-analytic model.

Economic evaluation

Results show that the use of AI-CVCs instead of standard CVCs can lead to a reduction in CRBSIs and decreased medical costs. Using the constructed decision-analytic model, the incremental cost per patient was estimated to be equal to –£138.20; that is, for every patient who receives an AI-CVC, there is an estimated cost-saving of £138.20. The results of a series of multivariate sensitivity analyses reveal that estimates of potentially large cost-savings, depending on the size of the population, may be anticipated under a wide range of cost and clinical assumptions. However, when considering the purchase of AI-CVCs, decision-makers in the NHS should ensure that their patient populations and the important characteristics of local clinical practice are indeed similar to those described in this economic evaluation.

Conclusions

The use of AI-CVCs reduces the rates of CRBSI for durations of between 5 and 12 days and greater than 20 days when CVCs are inserted in the femoral or jugular veins. Studies report the ▶

best clinical effect when CVCs are treated with minocycline rifampicin or internally and externally treated with silver or CHSS. Further evidence is needed to confirm or refute the benefits of externally treated catheters, most notably the catheters treated with CHSS.

Further evidence is required to test whether AI-CVCs reduce CRBSI for durations of between 13 and 20 days, for CVCs inserted into the subclavian vein and comparing catheters with different treatments.

Current published evidence suggests that AI-CVCs are cost-effective for high-risk patients compared with standard CVCs. However, given the paucity of the economic evidence available, the results of these studies must be interpreted carefully. A simple decision model estimated ICERs for a range of different assumptions and demonstrated that all reasonable scenarios show AI-CVCs to be dominant; that is, in terms of cost-effectiveness, they are cheaper and more effective.

However, the limitations of this review should be recognised. Local decisions as to whether or not to adopt AI-CVCs for the prevention of CRBSIs require a clear understanding of the evidence-based reviews and guideline recommendations as well as knowledge of local clinical practice and infection rates.

Overall, AI-CVCs are clinically effective and relatively inexpensive and therefore their integration into standard care can be justified. However, the use of these anti-infective catheters without the appropriate use of other practical care initiatives will have only a limited effect on the prevention of CRBSIs.

Recommendations for further research

It has been estimated that, to take account of all relevant clinical parameters, including mortality, related to the effectiveness of AI-CVCs, a single clinical trial would have to include around 10,000 patients in each study arm. It is highly unlikely that such a trial will ever be funded.

Comparative trials are required to determine which, if any, of the treated catheters is the most effective.

This review has demonstrated that AI-CVCs can be effective in reducing the number of CRBSIs compared with standard CVCs. Results of the included studies also indicate that rates of CRBSI can be minimised when standard CVCs are used. Therefore, recommendations for pragmatic research related to the effectiveness of bundles of care that may be effective in reducing rates of CRBSI are warranted. Such research will require local audit of CRBSI rates as well as the assessment of current care practices to evaluate the clinical effectiveness and cost-effectiveness of implementing a package of care to reduce CRBSI rates.

Publication

Hockenhull JC, Dwan K, Boland A, Smith G, Bagust A, Dündar Y, *et al*. The clinical effectiveness and cost-effectiveness of central venous catheters treated with anti-infective agents in preventing bloodstream infections: a systematic review and economic evaluation. *Health Technol Assess* 2008;**12**(12).

NIHR Health Technology Assessment Programme

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The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA Programme is needs-led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

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The research reported in this issue of the journal was commissioned by the HTA Programme as project number 05/38/01. The contractual start date was in October 2005. The draft report began editorial review in January 2007 and was accepted for publication in September 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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