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Major Article

Are antimicrobial peripherally inserted central catheters associated with reduction in central line-associated bloodstream infection? A systematic review and meta-analysis

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Background: Antimicrobial peripherally inserted central catheters (PICCs) may reduce the risk of central line-associated bloodstream infection (CLABSI). However, data regarding efficacy are limited. We aimed to evaluate whether antimicrobial PICCs are associated with CLABSI reduction.

Methods: MEDLINE, EMBASE, CINHAL, and Web of Science were searched from inception to July 2016; conference proceedings were searched to identify additional studies. Study selection and data extraction were performed independently by 2 authors.

Results: Of 597 citations identified, 8 studies involving 12,879 patients met eligibility criteria. Studies included adult and pediatric patients from intensive care, long-term care, and general ward settings. The incidence of CLABSI in patients with antimicrobial PICCs was 0.2% (95% confidence interval [CI], 0.0%-0.5%), and the incidence among nonantimicrobial catheters was 5.3% (95% CI, 2.6%-8.8%). Compared with noncoated PICCs, antimicrobial PICCs were associated with a significant reduction in CLABSI (relative risk [RR], 0.29; 95% CI, 0.10-0.78). Statistical heterogeneity (I^2, 71.6%; T2 = 1.07) was resolved by publication type, with peer-reviewed articles showing greater reduction in CLABSI (RR, 0.21; 95% CI, 0.06-0.74). Twenty-six patients (95% CI, 21-75) need to be treated with antimicrobial PICCs to prevent 1 CLABSI. Studies of adults at greater baseline risk of CLABSI experienced greater reduction in CLABSI (RR, 0.20; $P = .003$).

Conclusions: Available evidence suggests that antimicrobial PICCs may reduce CLABSI, especially in high-risk subgroups. Randomized trials are needed to assess efficacy across patient populations.

INTRODUCTION

Use of peripherally inserted central catheters (PICCs) in hospitalized patients and patients requiring long-term venous access has increased substantially during the past decade.[1,2] When it comes to central venous access, PICCs represent an advancement because they are easier and safer to insert, durable, and cost-effective compared with traditional central venous catheters (CVCs).[3-5] Like traditional CVCs, however, PICCs are associated with central line-associated bloodstream infection (CLABSI).[6-10] These infections are problematic because they increase morbidity, cost, duration of hospital stay, and mortality.[11]

In an effort to reduce CLABSI, strategies such as a checklist of best practices during catheter insertion and alcohol-and-chlorhexidine skin preparation have been introduced.[12] The recognition that CLABSI often occurs by migration of bacteria from the catheter entry site

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has also spurred the development of antimicrobial devices.[13] In systematic reviews, antimicrobial CVCs demonstrated substantial reduction in CLABSI, especially in immunocompromised and critically ill patients.[14,15] Although antimicrobial PICCs became commercially available around 2008, data regarding efficacy are limited. This gap is important because the use of PICCs is rapidly outpacing that of traditional CVCs.[9,16] Therefore, we performed a systematic review and meta-analysis to evaluate the effect of antimicrobial PICCs on CLABSI risk.

METHODS

Data sources and searches

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations when conducting this review.[17] We performed a comprehensive literature search for English and non-English language articles in multiple bibliographic databases (MEDLINE via Ovid, EMBASE, CINHAL, and Web of Science) from inception to July 2016. Literature searches used Boolean logic with terms that included *peripherally inserted central catheter*, *PICC*, *central line-associated blood stream infection*, and *antimicrobial or antiseptic-coated/impregnated* catheter. Additional records were identified by hand searches of bibliographies. We searched for ongoing clinical trials through clinicaltrials.gov and searched gray literature (eg, Google Scholar). We also searched select conference proceedings (Tables S1 and S2) from 2008 onward, because antimicrobial PICCs were not available before this period. All studies published in full text, abstract, or poster form were eligible for inclusion. Details regarding the search strategy are in the Appendix. The review was conducted in accordance with a published protocol (CRD-42015016958).

Study selection

We included studies that reported CLABSI or catheter colonization in hospitalized adult or pediatric patients, or patients requiring long-term venous access, who received an antimicrobial/antiseptic-coated or impregnated PICC compared with those who received noncoated PICCs. Two authors (RK and VC) independently assessed studies for eligibility. Discrepancies regarding eligibility were resolved by consensus. Study authors were contacted to request additional data when appropriate.

Data extraction and quality assessment

Data were extracted from included studies by independent reviewers (RK and VC) on a template adapted from the Cochrane Collaboration.[27] From each study we extracted the number of patients, patient population, rate or number of CLABSI or catheter colonization events, and definitions used to ascertain CLABSI. In addition, we abstracted device-specific data, including coating material (eg, minocycline-rifampin or chlorhexidine), PICC dwell time, and indication for placement. Study variables, including study design, comparator group, and allocation to a coated versus noncoated device, were also recorded.

Definition of comparison and treatment groups

Treatment groups were defined as patients who received antimicrobial-coated or impregnated PICCs for any clinical indication, whereas comparator groups included patients who received a noncoated or impregnated PICC. When studies included several types of CVC, we only included those where data specific to antimicrobial PICCs could be retrieved.

Definition of outcomes

The primary outcome was the occurrence of CLABSI or catheter colonization following PICC insertion (number of CLABSI events/number of catheters placed). Based on the data available, we abstracted both the absolute number of CLABSI events in patients and the rate of CLABSI per 1,000 catheter-days in patients who received coated versus noncoated devices.

Data synthesis and analysis

The unit of analysis was PICC insertion. Relative risk (RR) was calculated to compare CLABSI risk in patients who received coated catheters (numerator) to those with noncoated catheters (denominator). The Hartung-Knapp-Sidik-Jonkman random effects method was used for pooling estimates of effect, because it is preferable for meta-analyses with fewer than 10 studies.[28] When available, CLABSI rates (number of CLABSI events per catheter-days) were also pooled. To stabilize variance, the proportion of patients experiencing CLABSI (number of patients with CLABSI who had a PICC/number of patients with PICCs) were pooled using the Freeman-Tukey double arcsine transformation.[29]

As recommended by the Cochrane Handbook,[30] we explored heterogeneity between studies by τ^2 (between-study variance), Cochran's *Q*, and the I^2 statistic (variation in estimates attributable to heterogeneity). We classified heterogeneity as low, moderate, or high on the basis of an I^2 statistic of 25%, 50%, or 75%, respectively, according to the method suggested by Higgins and colleagues.[27] To evaluate publication bias, the Harbord test was used to assess funnel plot asymmetry.

We conducted prespecified subgroup analyses to establish whether coating type (chlorhexidine vs minocycline or rifampin), patient type (adult vs pediatric), patient location (acute care vs long-term care), and baseline risk of CLABSI (eg, general hospitalized vs burn, acute vs long-term care, or high-risk pediatric) affected results. In accordance with the literature, we classified studies involving patients with burns, cancer, or critical illness as high-risk populations, because these patients are at greater risk of CLABSI.[31,32]

Additional sensitivity analyses by study quality, publication type, sample size, and patient population were performed to assess robustness of our findings in accordance with published recommendations.[33] Random effects meta-regression was used to assess differences in RR across study types, using the Knapp-Hartung modification of variance.

Risk of bias assessment

Two authors independently evaluated risk of study bias on each of the included studies using the Newcastle-Ottawa Scale.[34] This instrument uses a star system to assess study quality in 3 domains: selection of study groups, comparability of groups, and ascertainment of outcomes. Only studies that received a star in each domain were designated low risk of bias (eg, high-quality studies). Studies that did not meet ≥1 criteria in each domain were classified as being at moderate or high risk of bias, respectively.

RESULTS

A total of 597 articles and conference abstracts were retrieved by our electronic and manual search (Fig 1). Of these citations, 9 articles (6 original peer-reviewed articles[18,19,22,24-26] and 3 conference abstracts[20,21,23]) met inclusion criteria. Two abstracts were combined because they reported data from the same cohort.[20,21] Therefore, after full review, 8 studies that included 12,879 patients were included in the systematic review.[18,19,21-26] Four studies