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Major article

Meta-analysis on central line–associated bloodstream infections associated with a needleless intravenous connector with a new engineering design

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Background: Intravenous needleless connectors (NCs) with a desired patient safety design may facilitate effective intravenous line care and reduce the risk for central line–associated bloodstream infection (CLA-BSI). We conducted a meta-analysis to determine the risk for CLA-BSI associated with the use of a new NC with an improved engineering design.

Methods: We reviewed MEDLINE, Cochrane Database of Systematic Reviews, Embase, ClinicalTrials.gov, and studies presented in 2010-2012 at infection control and infectious diseases meetings. Studies reporting the CLA-BSIs in patients using the positive-displacement NC (study NC) compared with negative- or neutral-displacement NCs were analyzed. We estimated the relative risk of CLA-BSIs with the study NC for the pooled effect using the random effects method.

Results: Seven studies met the inclusion criteria: 4 were conducted in intensive care units, 1 in a home health setting, and 2 in long-term acute care settings. In the comparator period, total central venous line (CL) days were 111,255; the CLA-BSI rate was 1.5 events per 1,000 CL days. In the study NC period, total CL days were 95,383; the CLA-BSI rate was 0.5 events per 1,000 CL days. The pooled CLA-BSI relative risk associated with the study NC was 0.37 (95% confidence interval, 0.16-0.90).

Conclusion: The NC with an improved engineering design is associated with lower CLA-BSI risk.

Health care workers (HCWs) risk accidental needlestick injuries and potential infection with bloodborne pathogens (BBPs) such as hepatitis B or C viruses or HIV when they use needles in conjunction with intravenous (IV) therapy. With the emergence of HIV infections and AIDS in the 1980s, HCWs, their unions, and U.S. federal and state agencies that regulate occupational safety and health became concerned about the potential risk of BBP infection among HCWs. As a result, in 1992, the U.S. Occupational Safety and Health Administration recommended that health care facilities use engineering controls to help protect HCWs from these pathogens. The use of such controls, including IV needleless connector (NC) systems, when applicable, became mandatory under the Needlestick Safety and Prevention Act in 2001. The NCs that we see today evolved from the industry's initial efforts to make devices that comply with these Occupational Safety and Health Administration regulations. They were primarily designed for HCW safety, to prevent accidental needlestick injuries and BBP infections. With the initial introduction of split septum NCs, outbreaks of central line–associated bloodstream infections (CLA-BSIs) occurred.[1] With the re-emphasis on the importance of infection control practices with these devices (eg, septum disinfection, cap changes, etc), infection

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Conflicts of interest: There was no specific grant for this study. Authors of this meta-analysis include employees of CareFusion and a clinical expert who provides consulting services to Baxter, CareFusion, Gojo, and Johnson and Johnson. He served as an unpaid clinical consultant and a coauthor for this article.

Additional information: None of these authors of the studies included in the meta-analysis were (or are) CareFusion employees or received financial support from CareFusion, the manufacturer of the study NC device. None of the studies in the meta-analysis were funded by CareFusion.

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risk was lowered. To further decrease the risk of needle use with such devices, negative displacement mechanical NCs were introduced. Then, to reduce the risk of CLA-BSIs and IV line occlusions, positive-displacement NCs were introduced. This led to a number of CLA-BSI outbreaks associated with some of these NCs.[2-5] Ultimately, this led to the Food and Drug Administration (FDA) requesting that U.S. manufacturers of positive-displacement NCs provide data that their devices were associated with risk of CLA-BSI at or below the level associated with negative-displacement NCs.

Newer generations of NCs have been designed with the intention of improving patient safety, specifically, reducing CLA-BSI risks. These design features include the following: a visible fluid path so that clinicians can assess the efficacy of their flush technique; a solid, flat, smooth access surface that can be effectively disinfected; a 1-part activation of the fluid path for effective flush; an open fluid pathway to provide a high flow rate and avoid hemolysis; and other desired safety features (eg, tight septum seal, minimal internal complexity, ability to flush with saline alone).[6-8] In spite of the improved design, there has been no systemic analysis on its associated CLA-BSI risk. We conducted an integrative review of the literature and meta-analysis to determine the risk of CLA-BSIs associated with the use of the new NC.

METHODS

Data sources

We developed research protocol and data collection tools consistent with the recommendations per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[9] We searched the MEDLINE database for relevant studies published from January 2006-December 2012. We also searched ClinicalTrials.gov, Embase, and the Cochrane Database of Systematic Reviews. Because the study NC was relatively new and published studies were scant, we extended the scope of the search to include published abstracts from a comprehensive list of major relevant infection control, infusion therapy, and infectious diseases scientific meetings where early data could be presented and identified. We performed Internet searches to locate relevant studies presented at the following research meetings (2010-2012): Association for Professionals in Infection Control and Epidemiology, Association for Vascular Access, Interscience Conference on Antimicrobial Agents and Chemotherapy, Infectious Disease Society of America, Infusion Nurses Society, National Home Infusion Association, The Fifth Decennial International Conference on Healthcare-Associated Infections, and Society for Healthcare Epidemiology of America.

Study selections and data extraction

Study inclusion criteria were randomized controlled trials or observational studies that reported the CLA-BSI rate in patients with the new MaxPlus positive-displacement connector (CareFusion, San Diego, CA) (study NC) compared with negative- or neutral-displacement NCs. We used the following Medical Subject Headings and key words: "*bloodstream* (*infection* OR *infections*) AND (*needleless connector*) OR (*mechanical valve*) OR (*needleless valve*) OR (*venous access*)" for the search. An Internet search was conducted independently by 2 investigators. All abstracts identified were read independently by 2 investigators (1 with a PhD, 1 with an MD). Disagreement was resolved by discussions with a third investigator. Data were extracted on standardized forms on study design, setting, patient population, facility location, number of CLA-BSIs (numerator), and number of central venous line (CL) days (denominator) during the study NC device versus comparator device periods for the studies included. We recorded CLA-BSI incidence density (infections per 1,000 CL days) at each site. We contacted authors to obtain the numerators and denominators when the study only reported the summary CLA-BSI rates.

Additional data regarding IV line care practices and the case mix index

To further evaluate potential risk factors associated with CLA-BSI, we contacted authors to obtain IV management and disinfection practices related to CLs during the study NC and comparator periods. These variables included use of a dedicated IV team, blood draws through the connector attached to the CL, type of disinfectants used in the cleaning of the NC, type of skin antiseptic used for CL placement and maintenance, maximum sterile barrier precaution usage, catheter securement method, and use of stopcocks in the line. Finally, we obtained the case mix index (CMI) from the Centers for Medicare and Medicaid Services as an aggregated measure of patient disease severity for each study site.[10-12]

Statistical analysis

Using the aggregated CLA-BSI rates during the comparators versus the study NC periods, we estimated the relative risk (RR) for CLA-BSIs associated with the study NC for each study. Then, we estimated the pooled effect using the random effects method.[13] For sensitivity analysis, we fit a random effect Poisson model with WinBUGS software (Cambridge Institute of Public Health, Cambridge, UK) for the pooled effect.[14] We further tested the impact of the time trend covariate on the RR estimate of the study NC. The Poisson model does not require normal distribution approximation for the effect of each study. It also applies when the number of events for a study is zero.[15] We used the Centers for Disease Control and Prevention's (CDC) Healthcare Infection Control Practices Advisory Committee review by Lee and Umscheid[16] and the U.S. FDA recommended methods[17] to compute a noninferiority margin allowing comparison against both a relative risk of 1.0 and a noninferiority margin.

We examined the distribution of the use of dedicated IV teams, blood draws in the line, choice of NC disinfectants, skin antiseptics used during CL insertion, use of maximum barrier precautions, methods of catheter securement, and use of stopcocks in the lines at each site. We examined whether any of these factors would influence the risk of CLA-BSI associated with the study NC, using the Poisson regression method.

Evaluation of heterogeneity across studies

To address the issue of potential heterogeneity and its impact on the estimate, we conducted systemic analyses.[9,18] We assessed heterogeneity between studies for the outcome using the Cochran Q statistic,[19] with $P \leq .10$ indicating significant heterogeneity,[20] and I^2, with suggested thresholds for low (25%-49%), moderate (50%-74%), and high (>75%) values.[21,22] We generated a funnel plot to determine study bias.[23-25] A funnel plot is a graph of the study effect (log scale of RR) plotted on the horizontal axis and a measure of within-study variance (standard error of log RR) on an inverted vertical axis.[26]

We also estimated the pooled effect by splitting 1 aggregated study[27] into 5 individual study sites because each site was geographically separate and consisted of independent patient populations and potentially different clinical practices.

RESULTS

Data synthesis

Published studies

A flow diagram outlining the search strategy and study selection for MEDLINE is shown in Figure 1A. Our search strategies produced