

Washington University School of Medicine Digital Commons@Becker

Open Access Publications

2007

Effect of chlorhexidine/silver sulfadiazine-impregnated central venous catheters in an intensive care unit with a low blood stream infection rate after implementation of an educational program: A before-after trial

Douglas J E Schuerer

Washington University School of Medicine in St. Louis

Ingrid B. Borecki

Washington University School of Medicine in St. Louis

David K. Warren

Washington University School of Medicine in St. Louis

Victoria J. Fraser

Washington University School of Medicine in St. Louis

John E. Mazuski

Washington University School of Medicine in St. Louis

Recommended Citation

Schuerer, Douglas J E; Borecki, Ingrid B.; Warren, David K.; Fraser, Victoria J.; Mazuski, John E.; Boyle, Walter A.; Buchman, Timothy G.; Coppersmith, Craig M.; and et al, "Effect of chlorhexidine/silver sulfadiazine-impregnated central venous catheters in an intensive care unit with a low blood stream infection rate after implementation of an educational program: A before-after trial." *Surgical infections*.8,4. 445-454. (2007).

http://digitalcommons.wustl.edu/open_access_pubs/3188

This Open Access Publication is brought to you for free and open access by Digital Commons@Becker. It has been accepted for inclusion in Open Access Publications by an authorized administrator of Digital Commons@Becker. For more information, please contact engeszer@wustl.edu.

See next page for additional authors

Follow this and additional works at: http://digitalcommons.wustl.edu/open_access_pubs

Authors

Douglas J E Schuerer, Ingrid B. Borecki, David K. Warren, Victoria J. Fraser, John E. Mazuski, Walter A. Boyle, Timothy G. Buchman, Craig M. Coppersmith, and et al

Effect of Chlorhexidine/Silver Sulfadiazine-Impregnated Central Venous Catheters in an Intensive Care Unit with a Low Blood Stream Infection Rate after Implementation of an Educational Program: A Before-After Trial*

DOUGLAS J.E. SCHUERER,¹ JEANNE E. ZACK,² JAMES THOMAS,³ INGRID B. BORECKI,⁴
CARRIE S. SONA,³ MARILYN E. SCHALLOM,³ MELISSA VENKER,²
JENNIFER L. NEMETH,³ MYRNA R. WARD,³ LINDA VERJAN,³ DAVID K. WARREN,⁵
VICTORIA J. FRASER,⁵ JOHN E. MAZUSKI,¹ WALTER A. BOYLE,⁶
TIMOTHY G. BUCHMAN,¹ and CRAIG M. COOPERSMITH¹

ABSTRACT

Background: Current guidelines recommend using antiseptic- or antibiotic-impregnated central venous catheters (CVCs) if, following a comprehensive strategy to prevent catheter-related blood stream infection (CR-BSI), infection rates remain above institutional goals based on benchmark values. The purpose of this study was to determine if chlorhexidine/silver sulfadiazine-impregnated CVCs could decrease the CR-BSI rate in an intensive care unit (ICU) with a low baseline infection rate.

Methods: Pre-intervention and post-intervention observational study in a 24-bed surgical/trauma/burn ICU from October, 2002 to August, 2005. All patients requiring CVC placement after March, 2004 had a chlorhexidine/silver sulfadiazine-impregnated catheter inserted (post-intervention period).

Results: Twenty-three CR-BSIs occurred in 6,960 catheter days (3.3 per 1,000 catheter days) during the 17-month control period. After introduction of chlorhexidine/silver sulfadiazine-impregnated catheters, 16 CR-BSIs occurred in 7,732 catheter days (2.1 per 1,000 catheter days; $p = 0.16$). The average length of time required for an infection to become established after catheterization was similar in the two groups (8.4 vs. 8.6 days; $p = 0.85$). Chlorhexidine/silver sulfadiazine-impregnated catheters did not result in a statistically significant change in the microbiological profile of CR-BSIs, nor did they increase the incidence of resistant organisms.

Conclusions: Although chlorhexidine/silver sulfadiazine-impregnated catheters are useful in specific patient populations, they did not result in a statistically significant decrease in the CR-BSI rate in this study, beyond what was achieved with education alone.

*Some of the material contained herein was presented orally (no written abstract) at the 35th Critical Care Congress, Society of Critical Care Medicine, San Francisco, January 23, 2006.

Departments of ¹Surgery, ⁴Genetics, ⁵Internal Medicine, and ⁶Anesthesiology, Washington University School of Medicine, St. Louis, Missouri.

Departments of ²Hospital Epidemiology and Infection Control and ³Nursing Barnes-Jewish Hospital, St. Louis, Missouri.

THE U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) estimate that 250,000 catheter-related blood stream infections (CR-BSIs) occur annually in the United States [1], although the incidence of this complication differs among countries [2]. The mortality rate of CR-BSI is controversial, with estimates ranging from 0 to 35% [3–8]. Although the attributable mortality rate of a CR-BSI is unclear, these infections place a substantial burden on the health care system, because they increase length of stay [4,6–8] and have been estimated to cost as much as \$56,167 (in 1998 dollars) in an intensive care unit (ICU) patient [9].

Exposure to central venous catheters (CVCs) is common in ICU patients, with utilization rates ranging from 0.36 CVC days/total patient days in coronary care units to 0.83 CVC days/total patient days in cardiothoracic ICUs. Surgical and medical ICUs have rates of 0.63 and 0.52, respectively [10]. Despite the high rate of CVC utilization in ICUs, multiple studies have shown that most CR-BSIs are preventable, if not all. One successful strategy is the implementation of an educational program aimed at physicians, nurses, or the entire multidisciplinary ICU team [11–16]. These programs typically stress adherence to best-practice behaviors known to prevent CR-BSIs, including the use of full barrier precautions [17], 2% chlorhexidine skin preparation at the insertion site [18], appropriate hand hygiene [19,20], and specifying the anatomic site of CVC placement (preferably the subclavian vein, then internal jugular, lastly femoral vein) [21–23]. Whereas the decrease in CR-BSIs varies depending on which intervention is being studied, a recent study by Berenholtz et al. demonstrated almost complete elimination of CR-BSIs from a surgical ICU after initiation of a comprehensive prevention program [24].

Another tool to prevent CR-BSIs is the use of antiseptic- or antimicrobial-impregnated catheters. To date, there have been 19 randomized trials, three meta-analyses, and two cost-benefit analyses of the efficacy of either chlorhexidine/silver sulfadiazine- or minocycline/rifampin-impregnated catheters [25]. The majority of these studies demonstrated significant decreases in CR-BSI rates without the development of resistant organisms, regardless of

which catheter was used [26,27]. Of note, placement of antiseptic-impregnated catheters is effective in decreasing CR-BSI if evidence-based practices are adhered to, but infection rates are still higher than desired [28]. The accumulated weight of these studies has resulted in recommendations from the CDC [1], the Agency for Healthcare Research and Quality [29], and thought leaders in the field [30,31] to use antiseptic- or antimicrobial-impregnated catheters in select patient populations, although the efficacy of these devices has not been accepted universally [32].

Because antiseptic- or antimicrobial-impregnated catheters are more expensive than standard CVCs, but the attributable cost of an infection is much greater than the cost of a catheter, there has been substantial interest in determining at-risk populations that would benefit most from the use of these catheters. The CDC recommends that an antiseptic- or antimicrobial-impregnated CVC be placed “in adults whose catheter is expected to remain in place >5 days if, after implementing a comprehensive strategy to reduce rates of CR-BSI, the CR-BSI rate remains above the goal set by the individual institution based on benchmark rates and local factors” [1]. “Comprehensive strategy” is defined as an educational program directed toward those who insert and maintain CVCs, as well as usage of both maximum barrier precautions and 2% chlorhexidine for skin preparation for CVC insertion.

Few data exist currently on the efficacy of antiseptic- or antimicrobial-impregnated catheters in ICUs that have instituted the comprehensive strategy outlined by the CDC. The purpose of this study was to address that specific question—what is the utility of antiseptic- or antibiotic-impregnated catheters (specifically chlorhexidine/silver sulfadiazine-impregnated catheters) in an ICU with low infection rates after a successful educational program to prevent CR-BSI? Previously, we instituted educational and behavioral interventions designed to prevent CR-BSI [11,12], resulting in infection rates that were one-third the United States national average, as determined by the National Nosocomial Infections Surveillance (NNIS) system at the time of publication. To determine if there was additional efficacy in using chlorhexidine/silver

sulfadiazine-impregnated catheters despite our low CR-BSI rates, we studied the effect of inserting these catheters in all patients in our surgical ICU over an 18-month time span.

PATIENTS AND METHODS

Study location and patient population

Barnes-Jewish Hospital is a 1,344-bed tertiary-care, university-affiliated teaching hospital. All patients admitted to the surgical ICU between October 1, 2002, and August 31, 2005, were enrolled in the study. The surgical ICU admits all critically ill non-cardiothoracic and non-neurosurgical surgical and trauma patients. Between October, 2002 and March, 2003, the surgical ICU had 18 beds. After a three-month transition, when the number of beds was variable, the surgical ICU expanded to 24 beds in May, 2003. This is reflected in an increase in yearly admissions from 1,499 in 2003 to 1,636 in 2004. The average length of stay was constant throughout the study at 4.3 days, as were nursing staff ratios. Throughout the study, all patients admitted to the surgical ICU were followed prospectively by an infection control team and surveyed for blood stream infections. Data for this study were collected after completion of our published educational and behavioral interventions to prevent CR-BSI in the surgical ICU [11,12].

Demographic data (age, CVC duration, Acute Physiology and Chronic Health Evaluation [APACHE] II score, ICU and hospital length of stay, CVC insertion site) were retrieved from the Project IMPACT database (Cerner, Inc., Kansas City, MO). Demographic data from a patient were recorded only once, regardless of how many CVCs were inserted. Prior to March 2004, this database was incomplete for most months. Thus, the demographic data presented in the pre-intervention group that did not have routine placement of chlorhexidine/silver sulfadiazine-impregnated catheters consist of data from only three non-contiguous months. To determine whether the patient population in the surgical ICU changed over the course of the study, demographic data from patients admitted before

March, 2004 (pre-intervention) were compared and found to be similar to both the post-intervention group from March, 2004–August, 2005 (where data were collected on all patients for 18 months) and all admissions to the surgical ICU for a six-month period earlier in 2002 (data not shown).

Each infection was classified as primary or secondary according to the CDC definitions used in previous publications on CR-BSI from our institution. A CR-BSI was defined as (1) a pathogen isolated from blood culture not related to infection at another site; or (2) fever $>38.5^{\circ}\text{C}$, chills, or hypotension and either of the following: (a) A common skin contaminant isolated from two blood cultures drawn on separate occasions unrelated to infection at another site; or (b) a common skin contaminant isolated from a blood culture from a patient with a CVC for which the physician initiated antimicrobial therapy.

Updates on CR-BSI rates were reported monthly at the surgical ICU's quality improvement conference and were compared with both prior rates within the surgical ICU and the published NNIS rates. The study was approved by the Washington University School of Medicine Human Studies Committee, and informed consent was waived.

Study design

Patients admitted to the surgical ICU prior to March 2004 (pre-intervention group) had conventional CVCs placed. Although chlorhexidine/silver sulfadiazine-impregnated catheters have been available commercially for years, they were not available in the ICU during the pre-intervention period in accordance with hospital policy at the time. All patients admitted to the surgical ICU after March, 2004 who required CVC insertion had chlorhexidine/silver sulfadiazine-impregnated catheters (Arrowgard Blue Plus; Arrow International, Reading, PA) placed (post-intervention group, with the intervention defined as the placement of chlorhexidine/silver sulfadiazine-impregnated catheters in patients who required a CVC). These second-generation catheters have both external coating and internal impregnation. The fact that all patients received these

catheters was based on a decision that any CVC placed in the surgical ICU was likely to stay in place for five days, and therefore met the CDC criteria for placement of antiseptic-impregnated catheters. Of note, mandatory educational modules on how to prevent CR-BSI continued on a regular basis throughout the study for both physicians and nurses in the surgical ICU.

A pre-hoc decision was made that the primary endpoint would be CR-BSI rates for CVCs placed in the surgical ICU, whereas the CR-BSI rate for all CVCs was a secondary endpoint regardless of whether they were placed inside or outside the surgical ICU. The rationale behind this decision was to eliminate the confounding effect of non-impregnated CVCs placed in the operating room, emergency department, hospital wards, interventional radiology department, or another hospital in the primary analysis. When examining the secondary endpoint of CR-BSI rates regardless of where a CVC was placed, a potential confounder was that some CVCs were placed immediately prior to a patient's admission (in the operating room), whereas some (e.g., Hohn catheters; Bard Access Systems, Salt Lake City, UT) were placed weeks or months earlier. Because there was no way of knowing how long every one these devices had been in place, catheter days for all lines were calculated by convention, assuming they were placed on admission to the surgical ICU. The calculated CR-BSI rates presented for all CVCs therefore likely represent overestimates of the true infection rate. The CR-BSI rates were calculated as infections/1,000 catheter days for the duration of the study. Each day a patient had a CVC in place was counted as a catheter day, regardless of the number of CVCs a patient had at a given time (i.e., the small minority of patients with multiple catheters in place simultaneously was counted daily as representing one catheter day).

All CVCs placed in the surgical ICU throughout the study were inserted by residents, fellows, two full-time nurse practitioners, or attending physicians. The residents were from the departments of surgery (post-graduate year [PGY]-1 and -2), anesthesiology (PGY-1-3), or emergency medicine (PGY-2) during their sur-

gical ICU rotation. All procedures were supervised by surgery, anesthesiology, or pulmonary/critical care fellows or by the attending physicians (50% each from the departments of surgery or anesthesiology). Peripherally inserted catheters and arterial catheters were excluded from study analysis.

On the basis of the results in the pre-intervention group, described below, the study was powered to determine if antiseptic-impregnated catheters would result in a 60% decrease in CR-BSI (i.e., similar to that achieved with education alone) [11]. This was done using a base frequency of 0.00330 (23/6,960), an alpha of 0.05, 80% power, and an expected post-intervention group of 7,000 catheter days. With a one-tailed test, statistical significance would be demonstrated if the number of infections decreased to 9.

Statistical analysis

Data were analyzed using the statistical software program Prism 3.0 (GraphPad Software, San Diego, CA). Infection rates and contingency tables (i.e., when comparing insertion site in the pre- and post-intervention groups) were analyzed using the chi-square test. Demographic and microbiology comparisons between the pre- and post-intervention groups were performed using the Mann-Whitney U-test. An alpha <0.05 was considered statistically significant.

RESULTS

Patients

There were 4,630 patients admitted to the surgical ICU during the 35 months of the study: 2,079 in the 17 months from October, 2002 to February, 2004 (prior to the institution of chlorhexidine/silver sulfadiazine-impregnated catheters) and 2,551 in the 18 months from March 2004 to August 2005 (when all patients receiving a CVC had an antiseptic-impregnated catheter inserted). Throughout the study, slightly more than one-third of all CVCs were placed in the surgical ICU, whereas the remainder were inserted in other locations (e.g., operating room, emergency department,

interventional radiology department). Demographics were similar in the pre-intervention and post-intervention groups except for a slightly higher APACHE II score in the post-intervention group (Table 1). The majority of CVCs were placed in the internal jugular vein, but this was attributable predominantly to placement of CVCs in the operating room (where insertion was nearly exclusively in the internal jugular); the majority of CVCs inserted in the surgical ICU were placed in the subclavian vein (data not shown). Of note, simply having a CVC in place was a marker of illness severity throughout the study because patients who had a CVC had higher mean APACHE II scores (18.2 vs. 15.6) and longer mean lengths of stay (6.9 ± 1.1 vs. 4.3 ± 7.2 days) than those without CVCs.

Catheter-related BSI in CVCs placed in surgical ICU

An average of 49 CVCs were placed per month in the surgical ICU throughout the study (range 15 to 64). There were 23 CR-BSIs in 6,960 catheter days of CVCs placed in the surgical ICU in the pre-intervention group (3.3 per 1,000 catheter days). After the introduction of chlorhexidine/silver sulfadiazine-impregnated catheters, there were 16 CR-BSIs in 7,732 days (2.1 per 1,000 catheter days; $p = 0.16$). When examined over six-month increments,

the infection rates were variable throughout the study (Table 2).

The demographics of the patients who developed CR-BSI in CVCs placed in the surgical ICU were similar regardless of whether the infection was of a standard catheter or a chlorhexidine/silver sulfadiazine-impregnated catheter (Table 3). Length of stay and anatomic site of catheter insertion also were similar. The average length of time a surgical ICU-placed CVC was indwelling prior to the development of CR-BSI was more than eight days, which is substantially greater than the average length of time the "typical" CVC remained in place, considering that fewer than 20% of all CVCs were indwelling for longer than seven days (compare length of catheterization for all CVCs in Table 1 with the duration of catheterization in CVCs that became infected in Table 3). No statistically significant differences in microbial isolates were noted in infections of CVCs placed in the surgical ICU, regardless of whether the patient had a standard catheter or a chlorhexidine/silver sulfadiazine-impregnated catheter, with gram-positive organisms predominating in both groups (Table 4).

Catheter-related BSI in all CVCs

In addition to these infections of CVCs placed in the surgical ICU, there were six CR-BSIs in CVCs placed prior to patient arrival in the sur-

TABLE 1. DEMOGRAPHICS OF PATIENTS WITH CENTRAL VENOUS CATHETER

	Pre-intervention ^a	Post-intervention ^b	P value
Where catheter placed (%)			0.56
In surgical ICU	34	39	
Outside surgical ICU	66	61	
Age (years)	60.4 ± 0.7	58.9 ± 2.5	0.35
Mean catheter duration (days)	2.8 ± 1.0	3.6 ± 0.7	0.12
<7 days (%)	83	82.8	
7-10 days (%)	12.1	11.9	
>10 days (%)	4.9	5.3	
Mean APACHE II score	17.1 ± 1.2	18.2 ± 0.6	0.04
Mean ICU length of stay (days)	7.0 ± 0.8	6.9 ± 1.1	0.87
Mean hospital length of stay (days)	25.6 ± 2.9	26.6 ± 7.3	0.83
Insertion site (%)			0.85
Subclavian vein	35.5	39.3	
Internal jugular vein	57.3	52.6	
Femoral vein	7.2	8.1	

^aBased on sampling of three months on 161 patients.

^b $N = 1,480$ patients.

ICU = intensive care unit; APACHE = Acute Physiology and Chronic Health Evaluation.

TABLE 2. CR-BSI RATES AT SIX-MONTH INTERVALS OF CENTRAL VENOUS CATHETERS PLACED IN SURGICAL ICU

	Primary infections	CVC days	Infections/1,000 CVC days	Total rate for period: infections/1,000 CVC days
Pre-intervention				
October, 2002–March, 2003	4	2,343	1.7	
April, 2003–September, 2003	11	2,470	4.4	3.3
October, 2003–February, 2004 ^a	8	2,147	3.7	
Post-intervention				
March, 2004–August, 2004	2	2,578	0.8	
September, 2004–February, 2005	5	2,402	2.1	2.1
March, 2005–August, 2005	9	2,752	3.3	

^aFive-month interval.

CR-BSI = catheter-related blood stream infection; CVC = central venous catheter.

gical ICU in both the pre- and post-intervention groups. Among all CVCs, there were 29 infections in the pre-intervention group (4.2 per 1,000 catheter days) and 22 infections in the post-intervention group (2.7 per 1,000 catheter days, $p = 0.15$), including 16 of chlorhexidine/silver sulfadiazine-impregnated catheters placed in the surgical ICU and six of standard catheters placed elsewhere. By comparison, in 2004, the NNIS rate for surgical ICUs nationwide was 3.4 per 1,000 catheter days. At all times during the study, the CR-BSI rates were lower than the NNIS rates published for that year, despite the fact that NNIS rates have declined steadily over the past three years [10,33]. Of note, the rate of secondary blood stream infections did not change throughout the study, with 28 secondary BSIs in both the pre-intervention and post-intervention time periods.

DISCUSSION

This study demonstrates that placing chlorhexidine/silver sulfadiazine-impregnated

catheters in all surgical ICU patients requiring CVC insertion failed to result in a statistically significant decrease in CR-BSI rates below the already-low rates obtained as the result of a comprehensive educational program and adherence to best-practice behaviors. Despite examining a number of infection-related parameters and having more than 600 CVCs placed in each group, chlorhexidine/silver sulfadiazine-impregnated catheters had no statistically significant impact on any endpoint examined.

There is little question that antiseptic- or antibiotic-impregnated catheters can prevent infection when used in the proper circumstances, because the preponderance of published literature on the subject supports their use. As such, our data do not refute the CDC recommendation to use these catheters when a CVC is expected to be in place for five days, CR-BSI rates are above an institutional goal despite an educational program, and both maximum barrier precautions and 2% chlorhexidine skin preparation are used. What is unclear from the CDC recommendation is what constitutes an appro-

TABLE 3. DEMOGRAPHICS OF PATIENTS HAVING CATHETER-RELATED BLOOD STREAM INFECTIONS FROM CENTRAL VENOUS CATHETERS PLACED IN SURGICAL INTENSIVE CARE UNIT

	Pre-intervention	Post-intervention	P value
Mean age (years)	55.5 ± 17.5	55.2 ± 20.0	0.97
Male (%)	13 (56 %)	9 (56 %)	1.00
Mean catheter time prior to infection (days)	8.4 ± 2.9	8.6 ± 3.2	0.70
Insertion site (%)			0.14
Subclavian vein	17 (73.9)	8 (50.0)	
Internal jugular vein	5 (21.8)	8 (50.0)	
Femoral vein	1 (4.3)	0	

TABLE 4. MICROORGANISMS ISOLATED FROM PATIENTS WITH CATHETER-RELATED BLOOD STREAM INFECTIONS FROM CENTRAL VENOUS CATHETERS PLACED IN SURGICAL INTENSIVE CARE UNIT

	Pre-intervention (%)	Post-intervention (%)
Gram-positive bacteria	17 (73.9)	8 (50)
Coagulase-negative staphylococci	7	3
<i>Enterococcus faecalis</i>	7	3
<i>Enterococcus faecium</i> (vancomycin-resistant)	2	2
<i>Staphylococcus aureus</i> (methicillin-resistant)	1	0
Gram-negative bacteria	5 (21.8)	4 (25)
<i>Acinetobacter baumannii</i>	4	1
<i>Pseudomonas aeruginosa</i>	1	1
<i>Enterobacter cloacae</i>	0	1
<i>Serratia marcescens</i>	0	1
Yeast	1 (4.3)	4 (25)
<i>Aspergillus</i> spp.	1	0
<i>Candida albicans</i>	0	3
<i>Candida parapsilosis</i>	0	1

appropriate institutional goal. In light of the fact that published data indicate that CR-BSI can be eliminated, we made the determination that the goal infection rate for the surgical ICU at Barnes-Jewish Hospital should be zero. Thus, strict implementation of the CDC guidelines would result in our using antiseptic- or antibiotic-impregnated catheters (either chlorhexidine/silver sulfadiazine or minocycline/rifampin) for all patients expected to have a catheter in place longer than five days. However, our results do not provide compelling evidence to justify placing chlorhexidine/silver sulfadiazine-impregnated catheters, although we cannot determine if minocycline/rifampin-impregnated catheters would have yielded similar results, nor can we rule out a true difference with chlorhexidine/silver sulfadiazine catheters that this study was not powered to detect.

The demographics of all patients with CVCs were strikingly similar throughout the 35 months of the study, as were the characteristics of the patients whose catheters became infected, regardless of whether the devices were chlorhexidine/silver sulfadiazine-impregnated. One interesting note was the non-significant trend toward more episodes of fungemia after the institution of chlorhexidine/silver sulfadiazine-impregnated catheters. Whereas numerous studies have demonstrated no change in infection patterns after the introduction of antiseptic- or antimicrobial-impregnated catheters, combining the data contained herein with those from

previous studies from our surgical ICU identified two episodes of fungemia over 56 months prior to the usage of chlorhexidine/silver sulfadiazine-impregnated catheters compared with four in the subsequent 18 months. Longer-term follow-up would be needed to determine the veracity of this finding, which still would not prove causality.

This study has a number of limitations. The first is simply our conclusion that there is no benefit in using chlorhexidine/silver sulfadiazine-impregnated catheters in an ICU where infection rates already are low following an educational program and compliance with best-practice behaviors. Despite there being 800 additional catheter days in the post-intervention group, there were seven fewer infections, a 30% decrease in the rate of BSI. Our conclusion of non-significance is based solely on the pre-determined establishment of an alpha of <0.05 . Because our previous educational program decreased CR-BSI rates more than 70%, we powered this study to detect a similar decrease in infections, not a 30% decrease. Clearly, if chlorhexidine/silver sulfadiazine-impregnated catheters actually decrease CR-BSI rates by 30%, this would be both biologically meaningful and cost-effective, even though it would not have been identified by the present study. With our low baseline BSI rate, a power analysis indicates that more than 35,000 catheter days would have been required in both the pre-intervention and the post-intervention groups to demonstrate a decrease of 30% in the CR-BSI

rate. Such power is not feasible in a single-institution study. Because the study was designed to only look for a major decrease in CR-BSI, it is possible that it fails to recognize the significance of a more modest decrease in infection rates, even if one is truly present. The substantial variability of our infection rates from month to month (Table 2), although we minimized this variability as much as possible by comparing aggregate data from 17 months pre-intervention and 18 months post-intervention, means that observation over a different time period might have yielded a different result.

Other limitations exist in the study design. Compared with a randomized trial, a pre/post study is susceptible to temporal bias attributable to unrecognized changes in patient populations or ICU practices. This study also could have been biased toward the intervention group, because there was no blinding to the use of the chlorhexidine/silver sulfadiazine-impregnated catheters. Further, we made the a priori decision that all CVCs placed in the surgical ICU had a substantial chance of being in place for five days to meet the CDC recommendation for antiseptic or antimicrobial catheter placement. However, the data presented in Table 1 demonstrate that more than 80% of the CVCs in the surgical ICU were in place for fewer than seven days. This discrepancy is not as great as it might seem, because the majority of CVCs were placed outside the surgical ICU, and these were likely to be in place for a shorter time than catheters placed in the surgical ICU because CVCs placed in the emergency department are considered contaminated by convention and are removed within 24–48 h, whereas catheters placed in the operating room frequently are intended for intra-operative monitoring and are removed shortly after surgery if no major complications occur. In contrast, CVCs placed in the surgical ICU generally are placed because long-term (e.g., parenteral nutrition) or reliable access (e.g., vasopressor therapy, determination of intravascular volume status) is needed, which makes it more likely that a CVC placed in the surgical ICU will be present for longer than five days. Nonetheless, some unknown percentage of CVCs placed in the surgical ICU during this study were likely to have been removed within five days, which

could confound our results. This difference in duration depending on where a catheter was placed (e.g., emergency department, surgical ICU) likely explains why more than 60% of the CVCs were placed outside the surgical ICU and yet infections in these non-antibiotic-impregnated catheters made up only a small percentage of the overall CR-BSI in both the pre-intervention and the post-intervention group. The lack of demographic data for 14 of 17 months in the pre-intervention group also is a limitation. Although the demographic data for three non-contiguous months were similar to those for the post-intervention group (and to those from the six months prior to the start of this study), we cannot rule out a transient change in patient population in 2003 that could have affected the results of this study. It is important to note that whereas some demographic data are missing for the pre-intervention group, the infection data were obtained using a different database and reflect accurately all 4,630 patients and 14,692 catheter days throughout the duration of the study.

A final limitation is the catheter used. Whereas there are substantial data supporting the benefit of chlorhexidine/silver-sulfadiazine-impregnated catheters [34–36], there also are studies that do not demonstrate a significant decrease in CR-BSI with their usage [37–39]. Because minocycline/rifampin-impregnated catheters have been shown to be superior to first-generation chlorhexidine/silver sulfadiazine-impregnated catheters [40], it is possible that different results would have been obtained had we used minocycline/rifampin-impregnated catheters.

Despite these limitations, this study has important implications for ICUs that have been successful in decreasing CR-BSI rates below NNIS averages, but have been unable to bring their rates to zero. In the subset of ICUs that have CR-BSI rates below the NNIS rate, our data indicate that inserting chlorhexidine/silver sulfadiazine-impregnated catheters in all patients does not result in a significant decrease in infections (the study was not powered to demonstrate a smaller effect). Additional studies are needed in different ICUs and with different catheters to determine the generalizability of these findings.

ACKNOWLEDGMENTS

The authors thank the entire staff of the 84ICU. This work was supported by funding from the Centers for Disease Control and Prevention (UR8/CCU715087-04 and R01CI000206-01) and the National Institutes of Health (K23AI-050585).

REFERENCES

- O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. *MMWR Recomm Rep* 2002;51:1-29.
- Merrer J. [Epidemiology of catheter-related infections in intensive care unit](Fre). *Ann Fr Anesth Reanim* 2005;24:278-281.
- Wenzel RP, Edmond MB. The impact of hospital-acquired bloodstream infections. *Emerg Infect Dis* 2001;7:174-177.
- Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients: Excess length of stay, extra costs, and attributable mortality. *JAMA* 1994;271:1598-1601.
- Smith RL, Meixler SM, Simberkoff MS. Excess mortality in critically ill patients with nosocomial bloodstream infections. *Chest* 1991;100:164-167.
- Digiiovine B, Chenoweth C, Watts C, Higgins M. The attributable mortality and costs of primary nosocomial bloodstream infections in the intensive care unit. *Am J Respir Crit Care Med* 1999;160:976-981.
- Soufir L, Timsit JF, Mahe C, et al. Attributable morbidity and mortality of catheter-related septicemia in critically ill patients: A matched, risk-adjusted, cohort study. *Infect Control Hosp Epidemiol* 1999;20:396-401.
- Rello J, Ochagavia A, Sabanes E, et al. Evaluation of outcome of intravenous catheter-related infections in critically ill patients. *Am J Respir Crit Care Med* 2000;162:1027-1030.
- Dimick JB, Pelz RK, Consunji R, et al. Increased resource use associated with catheter-related bloodstream infection in the surgical intensive care unit. *Arch Surg* 2001;136:229-234.
- National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004 (issued October 2004). *Am J Infect Control* 2004;32:470-485.
- Coopersmith CM, Rebmann TL, Zack JE, et al. Effect of an education program on decreasing catheter-related bloodstream infections in the surgical intensive care unit. *Crit Care Med* 2002;30:59-64.
- Coopersmith CM, Zack JE, Ward MR, et al. The impact of bedside behavior on catheter-related bacteremia in the intensive care unit. *Arch Surg* 2004;139:131-136.
- Sherertz RJ, Ely EW, Westbrook DM, et al. Education of physicians-in-training can decrease the risk for vascular catheter infection. *Lancet* 2000;355:641-648.
- Eggimann P, Harbarth S, Constantin MN, et al. Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. *Lancet* 2000;355:1864-1868.
- Slater F. Cost-effective infection control success story: A case presentation. *Emerg Infect Dis* 2001;7:293-294.
- Bijma R, Girbes AR, Kleijer DJ, Zwaveling JH. Preventing central venous catheter-related infection in a surgical intensive-care unit. *Infect Control Hosp Epidemiol* 1999;20:618-620.
- Raad II, Hohn DC, Gilbreath BJ, et al. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *Infect Control Hosp Epidemiol* 1994;15:231-238.
- Maki DG, Ringer M, Alvarado CJ. Prospective randomized trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet* 1991;338:339-343.
- Doebbeling BN, Stanley GL, Sheetz CT, et al. Comparative efficacy of alternative hand-washing agents in reducing nosocomial infections in intensive care units. *N Engl J Med* 1992;327:88-93.
- Maury E, Alzieu M, Baudel JL, et al. Availability of an alcohol solution can improve hand disinfection compliance in an intensive care unit. *Am J Respir Crit Care Med* 2000;162:324-327.
- Merrer J, De Jonghe B, Golliot F, et al. Complications of femoral and subclavian venous catheterization in critically ill patients: A randomized controlled trial. *JAMA* 2001;286:700-707.
- Mermel LA. Prevention of intravascular catheter-related infections. *Ann Intern Med* 2000;132:391-402.
- Goetz AM, Wagener MM, Miller JM, et al. Risk of infection due to central venous catheters: Effect of site of placement and catheter type. *Infect Control Hosp Epidemiol* 1998;19:842-845.
- Berenholtz SM, Pronovost PJ, Lipsett PA, et al. Eliminating catheter-related bloodstream infections in the intensive care unit. *Crit Care Med* 2004;32:2014-2020.
- Crnich CJ, Maki DG. Are antimicrobial-impregnated catheters effective? When does repetition reach the point of exhaustion? *Clin Infect Dis* 2005;41:681-685.
- Marin MG, Lee JC, Skurnick JH. Prevention of nosocomial bloodstream infections: Effectiveness of antimicrobial-impregnated and heparin-bonded central venous catheters. *Crit Care Med* 2000;28:3332-3338.
- Veenstra DL, Saint S, Saha S, et al. Efficacy of antiseptic-impregnated central venous catheters in preventing catheter-related bloodstream infection: A meta-analysis. *JAMA* 1998;281:261-267.
- Frankel HL, Crede WB, Topal JE, et al. Use of corporate Six Sigma performance-improvement strategies to reduce incidence of catheter-related bloodstream infections in a surgical ICU. *J Am Coll Surg* 2005;201:349-358.

29. Agency for Healthcare Research and Quality. Making healthcare safer: A critical analysis of patient safety practices. Rockville, MD, 2001.
30. Crnich CJ, Maki DG. Are antimicrobial-impregnated catheters effective? Don't throw out the baby with the bathwater. *Clin Infect Dis* 2004;38:1287-1292.
31. McGee DC, Gould MK. Preventing complications of central venous catheterization. *N Engl J Med* 2003;348:1123-1133.
32. McConnell SA, Gubbins PO, Anaissie EJ. Do antimicrobial-impregnated central venous catheters prevent catheter-related bloodstream infection? *Clin Infect Dis* 2003;37:65-72.
33. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2003 (issued August 2003). *Am J Infect Control* 2003;31:481-498.
34. Maki DG, Stolz SM, Wheeler S, Mermel LA. Prevention of central venous catheter-related bloodstream infection by use of an antiseptic-impregnated catheter. A randomized, controlled trial. *Lancet* 1997;127:257-266.
35. George SJ, Vuddamalay P, Boscoe MJ. Antiseptic-impregnated central venous catheters reduce the incidence of bacterial colonization and associated infection in immunocompromised transplant patients. *Eur J Anaesthesiol* 1997;14:428-431.
36. van Heerden PV, Webb SA, Fong S, et al. Central venous catheters revisited: Infection rates and an assessment of the new Fibrin Analysing System brush. *Anaesth Intensive Care* 1996;24:330-333.
37. Heard SO, Wagle M, Vijayakumar E, et al. Influence of triple-lumen central venous catheters coated with chlorhexidine and silver sulfadiazine on the incidence of catheter-related bacteremia. *Arch Intern Med* 1998;158:81-87.
38. Sheng WH, Ko WJ, Wang JT, et al. Evaluation of antiseptic-impregnated central venous catheters for prevention of catheter-related infection in intensive care unit patients. *Diagn Microbiol Infect Dis* 2000;38:1-5.
39. Tennenberg S, Lieser M, McCurdy B, et al. A prospective randomized trial of an antibiotic- and antiseptic-coated central venous catheter in the prevention of catheter-related infections. *Arch Surg* 1997;132:1348-1351.
40. Darouiche RO, Raad II, Heard SO, et al. A comparison of two antimicrobial-impregnated central venous catheters. Catheter Study Group. *N Engl J Med* 1999;340:1-8.

Address reprint requests to:

Dr. Craig M. Coopersmith

Washington University School of Medicine

660 South Euclid Ave.

Campus Box 8109

St. Louis, MO 63110

E-mail: coopersthc@wustl.edu