Health Care–Associated Bloodstream Infections Associated with Negative- or Positive-Pressure or Displacement Mechanical Valve Needleless Connectors

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Background. Health care–associated, central venous catheter–related bloodstream infections (HA-BSIs) are a major cause of morbidity and mortality. Needleless connectors (NCs) are an important component of the intravenous system. NCs initially were introduced to reduce health care worker needlestick injuries, yet some of these NCs may increase HA-BSI risk.

Methods. We compared HA-BSI rates on wards or intensive care units (ICUs) at 5 hospitals that had converted from split septum (SS) connectors or needles to mechanical valve needleless connectors (MV-NCs). The hospitals (16 ICUs, 1 entire hospital, and 1 oncology unit; 3 hospitals were located in the United States, and 2 were located in Australia) had conducted HA-BSI surveillance using Centers for Disease Control and Prevention definitions during use of both NCs. HA-BSI rates and prevention practices were compared during the pre-MV period, MV period, and post-MV period.

Results. The HA-BSI rate increased in all ICUs and wards when SS-NCs were replaced by MV-NCs. In the 16 ICUs, the HA-BSI rate increased significantly when SS-NCs or needles were replaced by MV-NCs (6.15 vs 9.49 BSIs per 1000 central venous catheter [CVC]–days; relative risk, 1.54; 95% confidence interval, 1.37–1.74; P<.001). The 14 ICUs that switched back to SS-NCs had significant reductions in their BSI rates (9.49 vs 5.77 BSIs per 1000 CVC–days; relative risk, 1.65; 95% confidence interval, 1.38–1.96; P<.001). BSI infection prevention strategies were similar in the pre-MV and MV periods.

Conclusions. We found strong evidence that MV-NCs were associated with increased HA-BSI rates, despite similar BSI surveillance, definitions, and prevention strategies. Hospital personnel should monitor their HA-BSI rates and, if they are elevated, examine the role of newer technologies, such as MV-NCs.

Each year in the United States, >150 million intravascular (IV) catheters are used. IV catheters are the major risk factor for health care–associated catheter-related bloodstream infections (HA-BSIs). HA-BSIs result in substantial morbidity and mortality and cost $34,000–$56,000 per episode [1–3]. The Centers for Disease Control and Prevention (CDC) estimates that, in US intensive care unit (ICU) patients, >80,000 HA-BSIs occur, costing up to $29 billion annually [1, 4, 5]. In October 2008, the Center for Medicare and Medicaid Services (CMS) and major US health insurance carriers discontinued increased payment for HA-BSIs, so HA-BSI prevention is even more critical for facility financial viability.

Needles used with IV catheters are a source of health care worker (HCW) needlestick injuries (NSIs). In 1992, the US Occupational Safety and Health Administration recommended that health care facilities use safer IV devices to protect HCWs. The first generation of these devices introduced were needle devices with...
shielding or retracting mechanisms, which provide protection during and after use. The second generation were split septum (SS) needleless connectors (NCs), in which a blunt cannula is used to access the connector rather than a needle. The third generation were mechanical valve (MV) NCs that generate negative, positive (eg, positive displacement, positive bolus or positive pressure), or neutral pressure during disconnect, and the MV-NC is accessed using luer lock connectors, thereby eliminating needle use.

When SS-NCs were first introduced, several HA-BSI outbreaks occurred [6–8]. Risk factors for HA-BSIs are poor adherence to infection control practices and the lack of HCW education and training [6, 7]. Since practice improvement, SS-NCs have been used for >15 years with low rates of HA-BSI. During the past decade, there has been the gradual introduction, first in the United States and then worldwide, of a wide variety of negative, positive, or neutral pressure MV-NCs. The true impact of these MV-NCs on patient safety is unknown. To date, 4 HA-BSI outbreaks temporally associated with the introduction of positive pressure MV-NCs have been reported [9–12]. We report increased HA-BSIs occurring at hospitals in the United States and Australia associated with the introduction of several different negative- or positive-pressure MV-NCs.

PATIENTS AND METHODS

In response to a report of increased HA-BSIs temporally associated with switching from SS-NCs to MV-NCs at the Society for Healthcare Epidemiology of America (SHEA) annual meeting in April 2004 (K. Hall, personnel communication), we attempted to identify whether other health care facilities had similar experiences using a quasi-experimental study design. Focus groups were organized at national and international infection control and infectious diseases meetings to discuss the experiences of various health care institutions when switching from needle/SS-NCs to MV-NCs. In addition, other health care facility personnel approached several of the authors after HA-BSI presentations to report experiencing an increase in HA-BSIs temporally associated with the introduction of MV-NCs. Those attending the focus groups used a variety of MV-NCs. Those who had prospectively collected active surveillance HA-BSI rate data during the SS-NC and MV-NC periods were invited to collaborate. Surveillance for HA-BSIs at all collaborating hospitals was conducted by their infection preventionists (IPs) using the same (ie, CDC) definitions, data collection processes, and methods during all study periods. All HA-BSI data had been obtained before the focus group meetings. The pre–MV-NC period was defined as the period when only SS-NCs or needles (in 1 facility) were used. The MV-NC period was the period when only SS-NCs were used. The post–MV-NC period was the period after discontinuation of the use of MV-NCs when some hospitals reverted to SS-NC use. The HA-BSI rates for the various NC periods were compared using the \( \chi^2 \) test; relative risks and 95% confidence intervals were calculated using Epi Info, version 3.3 (CDC).

To evaluate factors responsible for switching from SS-NC to MV-NC, collaborators were asked who had made the decision at their facility and how the decision had been made. In addition, because HA-BSI prevention practices influence HA-BSI rates, we assessed HA-BSI prevention practices (Table 1).

RESULTS

HA-BSI prevention infection control practices. All collaborators conducted active surveillance for HA-BSIs using CDC definitions and surveillance methods [13, 14]. All HA-BSI rate data had been collected prospectively during patient admissions for all periods by each facility’s IPs before our focus group meetings/collaboration. HA-BSI prevention practices were similar for all the participating health care facilities (Table 1). During both periods, the majority used recommended HA-BSI prevention “bundles,” including HCW hand hygiene, chlorhexidine gluconate for patient skin antisepsis, maximum barrier precautions for catheter insertion, and alcohol for NC disinfection. Data were provided by IPs at 5 hospitals (4 academic and 1 community hospital), including 16 ICUs, hospital-wide (hospital C), and 1 adult oncology ward (hospital D). During the study periods, there were no changes in HA-BSI surveillance or IV clinical practices, patient populations, patient culturing for BSI symptoms, nurse-to-patient ratios, or IPs.

Drivers for NC change. Reasons for changing from SS- to MV-NCs varied and included: to reduce needle use, to better visualize the NC internal structure (ie, through the use of translucent MV-NCs), concern that SS-NCs would no longer be manufactured, use of an infusion pump requiring manufacturer-compatible IV consumables (including an MV-NC), or to reduce prophylactic heparin/thrombolytic agent use. Often, the decision to change from SS- to MV-NC was made by occupational health, product evaluation, or other committees, without infection control personnel input.

MV-NC introduction. Participating health care facilities switched from SS-NCs \((n = 4)\) or needle \((n = 1)\) to MV-NCs from several manufacturers (Table 2). Participants used either the Interlink (Baxter Healthcare) SS-NC \((n = 4)\) or needles \((n = 1)\) before MV-NC introduction. The introduced MV-NC manufacturers included: 1 negative-pressure MV-NC (Clearlink; Baxter Healthcare) \((n = 2)\) and 3 positive pressure MV-NCs (UltraSite; B. Braun Medical) \((n = 1)\) or SmartSite (Cardinal Health, previously Alaris Medical Systems) \((n = 2)\). Data were available for 6–24 months (median period, 18 months; mean period, 15.6 months) of pre-MV-NC use and 11–39 months (median period, 12 months; mean period, 18.8 months) of MV-NC use.
<table>
<thead>
<tr>
<th>Hospital</th>
<th>IV team</th>
<th>Antibiotic/antiseptic impregnated catheters</th>
<th>CHG patch (eg, BioPatch)</th>
<th>Catheter securement device (eg, Statlock)</th>
<th>Vancomycin prophylaxis</th>
<th>Use of stopcocks in IV line</th>
<th>Blood draws through NC</th>
<th>NC disinfectant</th>
<th>SS period: use of maximum barrier precautions</th>
<th>SS period skin antiseptic for CVC placement</th>
<th>MV period: use of maximum barrier precautions</th>
<th>MV period: skin antiseptic for CVC placement</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>Yes&lt;sup&gt;a&lt;/sup&gt;</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>ETOH</td>
<td>Yes</td>
<td>ETOH/PI</td>
<td>Yes</td>
<td>CHG/ETOH</td>
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<tr>
<td>B</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>ETOH</td>
<td>No</td>
<td>ETOH/PI</td>
<td>Yes</td>
<td>CHG</td>
<td>CHG</td>
</tr>
<tr>
<td>C</td>
<td>No</td>
<td>No&lt;sup&gt;b&lt;/sup&gt;</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>ETOH</td>
<td>CHG/ETOH</td>
<td>Yes</td>
<td>CHG/ETOH</td>
<td>CHG/ETOH</td>
</tr>
<tr>
<td>D</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>ETOH</td>
<td>Yes</td>
<td>CHG/ETOH</td>
<td>Yes</td>
<td>CHG/ETOH</td>
</tr>
<tr>
<td>E</td>
<td>No</td>
<td>SS period, no; MV period, yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>ETOH</td>
<td>Yes&lt;sup&gt;c&lt;/sup&gt;</td>
<td>CHG/ETOH</td>
<td>Yes</td>
<td>CHG/ETOH</td>
</tr>
</tbody>
</table>

**NOTE.** CHG, chlorhexidine gluconate; ETOH, alcohol; IV, intravenous; MV, mechanical valve; NC, needleless connector; PI, povidone iodine; SS, split septum.

<sup>a</sup> On wards but not in the intensive care unit; for peripheral catheters, but not central venous catheters.

<sup>b</sup> Some antiseptic-impregnated catheters used on the basis of patient risk.

<sup>c</sup> Yes, except uses drape covering half the body.
Comparison of pre-MV-NC and MV-NC HA-BSI rates. The HA-BSI rate increased in all ICUs and wards after switching from SS-NC/needles to MV-NCs. In the pre-MV-NC period, HA-BSI rates were 0–8.47 BSIs per 1,000 central venous catheter (CVC)- or patient-days (median value, 3.09; mean value, 3.80), whereas in the MV-NC period, the HA-BSI rate was 3.41–11.8 BSIs per 1000 CVC- or patient-days (median value, 6.20; mean value, 6.83) (Table 3). In each facility, increased HA-BSI rates were detected in all the individual units and wards surveyed. Four of 5 facilities and 9 of 18 specific wards or units had statistically significant increases in their HA-BSI rates in the MV-NC versus pre-MV-NC periods. When data from all 16 participating hospital ICUs were combined, there was a significant increase in the BSI rate when MV-NCs were introduced (pre-MV-NC period vs MV-NC period: 389 BSIs per 63,295 CVC-days [6.1 BSIs per 1000 CVC-days] vs 1104 BSIs per 116,317 CVC-days [9.5 BSIs per 1000 CVC-days]; $P<.001$).

Once increased HA-BSI rates were detected, current HA-BSI prevention strategies, including hand hygiene, CDC IV guideline recommendations, and HA-BSI prevention bundle elements, including NC aseptic manipulation disinfection, were repeatedly reinforced through education in all the involved units and wards. In some instances, HA-BSI rates decreased slightly, but the HA-BSI rate did not decrease to pre-MV-NC period rates at any of the facilities that continued to use the MV-NCs (data not shown).

The pathogens responsible for HA-BSI varied slightly among the 4 reporting facilities. For most hospitals, coagulase-negative staphylococci were the most common organism, followed by Staphylococcus aureus, yeast, enterococcus, and other gram-negative or gram-positive bacteria. In general, when hospitals changed from SS-NCs to MV-NCs, the proportion of HA-BSIs caused by yeast (4 hospitals), enterococci (2), or other gram-negative bacteria (2)—mostly Pseudomonas, Klebsiella and Enterobacter species increased.

Impact of reverting from MV-NCs to SS-NCs. At 3 health care facilities, when HA-BSI rates could not be reduced to pre-MV-NC rates and it was feasible to change the NCs, the MV-NCs were discontinued and initial or alternative SS-NCs were used. The post-MV-NC period ranged from 5 through 18 months (median period, 8 months; mean period, 10.3 months). In these facilities, the HA-BSI rates decreased to below the previous pre-MV-NC BSI rate (Table 3); at 3 facilities, the decrease in HA-BSI rate reached statistical significance (10 ICUs and 1 hospital [all wards]). When we combined the HA-BSI data for 14 ICUs where MV-NC use was discontinued and SS-NCs were reintroduced, there was a significant reduction in BSI rate (MV-NC period: 1104 BSIs per 116,317 CVC-days [9.5 BSIs per 1000 CVC-days] vs post-MV-NC period: 152 BSIs per 26,359 CVC-days [5.8 BSIs per 1000 CVC-days]; $P<.001$). The HA-BSI rates in the pre-MV SS-NC period and the post-MV-NC period at these hospitals were not statistically significantly different.

DISCUSSION

We describe increased HA-BSI rates temporally associated with changing from needles or SS-NCs to either negative- or positive-pressure MV-NCs on 13 wards or units in 4 hospitals and 1 entire hospital (4 ICUs and all wards) on 2 continents and in a variety of settings. Furthermore, in those reverting to SS-NCs, the HA-BSI rate substantially decreased.

Our study has several unique characteristics. First, to our knowledge, it is the largest, most comprehensive evaluation of MV-NCs and HA-BSI rates (multicenter, academic, and community settings; domestic and international; multiple MV-NCs) to date. Second, it is the first study to compare HA-BSI rates when using a variety of MV-NCs (both positive and negative pressure) and SS-NCs. Third, we systematically evaluated HA-BSI prevention practices employed during all study periods. Fourth, we evaluated reasons for changing from SS- to MV-NC. Fifth, we used a focus group collaborative method to obtain the above in-use data.

Previous publications of increased HA-BSI rates temporally associated with MV-NC use have been reported from >1 unit at single institutions; all involved positive pressure MV-NCs [9–12]. These outbreaks led to the SHEA–Infectious Diseases Society of America (IDSA) recently recommending against the routine use of positive pressure MV-NCs [15]. In contrast, our study documents an increased HA-BSI rate in a large number of different types of ICUs and wards in academic and community hospitals in 2 countries associated with a variety of negative- or positive-pressure MV-NCs produced by different manufacturers. This expands the list of MV-NCs associated..

### Table 2. Participants Split Septum (SS) and Mechanical Valve (MV) Needleless Connectors and Use Periods.

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Country</th>
<th>SS/needle used</th>
<th>Duration SS use, months</th>
<th>MV used</th>
<th>Duration of MV use, months</th>
<th>Device used</th>
<th>Duration post-MV period, months</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>United States</td>
<td>Interlink</td>
<td>18</td>
<td>UltraSite</td>
<td>39</td>
<td>O-Syte</td>
<td>8</td>
</tr>
<tr>
<td>B</td>
<td>United States</td>
<td>Interlink</td>
<td>24</td>
<td>Clearlink</td>
<td>21</td>
<td>Interlink</td>
<td>5</td>
</tr>
<tr>
<td>C</td>
<td>United States</td>
<td>Interlink</td>
<td>18</td>
<td>Clearlink</td>
<td>11</td>
<td>Interlink</td>
<td>18</td>
</tr>
<tr>
<td>D</td>
<td>Australia</td>
<td>Interlink</td>
<td>12</td>
<td>SmartSite</td>
<td>12</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>E</td>
<td>Australia</td>
<td>Needles</td>
<td>6</td>
<td>SmartSite</td>
<td>11</td>
<td>Not available</td>
<td>Not available</td>
</tr>
</tbody>
</table>
with increased risk of HA-BSIs and suggests that a broader range of negative- or positive-pressure MV-NCs may increase HA-BSI risk.

Previous studies have not described either the surveillance methods used or possible variation in HA-BSI prevention practices during the SS-NC and MV-NC periods. Such changes can influence HA-BSI rates. Our data indicate that HA-BSI prevention practices were equal or enhanced in the MV-NC period, compared with SS-NC period. Thus, inferior infection control practices alone cannot explain the increased HA-BSI risk. Although some facilities achieved a slight HA-BSI rate reduction with enhanced education, none achieved baseline HA-BSI rates. Furthermore, in 1 hospital, 31% of ICU clinicians did not disinfect the MV-NC before manipulation (T. Karchmer, personnel communication). Clinicians either may not be disinfecting or may be inadequately disinfecting MV-NCs. Although the rate of such practices may not have differed during the SS-NC and MV-NC periods, exposure of MV-NCs to blood and/or nutritional fluids enables biofilm development and enhances pathogen growth if contamination occurs.

Third, although infection control practices were similar in both periods, and clinician compliance was most likely similar (ie, not perfect), the impact of these breeches may be greater when MV-NCs are used. MV-NC device design may impact infection control efficacy. Menyhay and Maki [16] showed that when 70% alcohol was used as an MV-NC disinfectant for 3–5 sec, significant contamination remained in 67% of the cases. Furthermore, in 1 hospital, ~31% of ICU clinicians did not disinfect the MV-NC before manipulation (T. Karchmer, personnel communication). Clinicians either may not be disinfecting or may be inadequately disinfecting MV-NCs. Although the rate of such practices may not have differed during the SS-NC and MV-NC periods, exposure of MV-NCs to blood and/or nutritional fluids enables biofilm development and enhances pathogen growth if contamination occurs.

Fourth, most MV-NCs are opaque (with 1 exception; Clearlink is transparent), so that it is impossible to determine whether they have been flushed adequately after each use. Thus, if blood or nutritional fluids remain in the MV-NC and the device is contaminated by HCWs’ hands during use, the pathogen(s) transferred to the MV-NC can proliferate and subsequently cause HA-BSI. One study showed that, when the first 10 mL of blood withdrawn from the MV-NCs and IV line of ICU patients was cultured, ∼17% of specimens were culture positive (R. Sheretz, personnel communication). The data from our study and from previous studies show that HA-BSI organisms from patients with MV-NCs are a combination of potential contaminants (eg, coagulase-negative staphylococci) and true pathogens. These data suggest that, because of their more complex design, negative- or positive-pressure MV-NCs may be excessively susceptible to inadvertent contamination and inadequate disinfection, both of which can contribute to HA-BSI development.
Two points deserve emphasis. First, at several of the facilities, the HA-BSI rate increased several-fold (by as much as 25%–400%), yet when the MV-NC BSI and SS-NC BSI rates were compared, they did not reach statistical significance. This may reflect small sample sizes. At hospital A, where hospital-wide surveillance for HA-BSIs is performed, an increase in HA-BSIs was detected only because the entire hospital was being surveyed. The increase on any single unit or ward was small, which is consistent with intermittent contamination of the MV-NCs. This may explain why several facilities (especially small hospitals or units) had large increases in HA-BSIs, but the differences between HA-BSI rates during the SS-NC period and the MV-NC period were not statistically significant. Thus, those evaluating HA-BSI rates, particularly at typical US community hospitals (which generally have <100 beds), should examine the magnitude of the increase in HA-BSIs, the pathogen distribution, and the HA-BSI rate. For those facilities with limited numbers of patients, the increase in the number of HA-BSIs (assuming a constant denominator) may suggest a problem even before a statistically significant increase in the rate of HA-BSIs is detected. This “small” number of excess HA-BSIs has important patient and facility economic consequences, because payers are increasingly paying for performance and eliminating enhanced payment for HA-BSIs [17].

In 3 participating facilities, where elevated HA-BSI rates could not be reduced despite multiple interventions, the use of SS-NCs was readopted; at these facilities, HA-BSI rates significantly decreased to levels at or below pre-MV-NC baseline levels. Because the IPs, surveillance methods, practices, and patient populations had not changed, the reduced HA-BSI rates can be attributable to the change of NCs used.

There are no other published long-term studies evaluating the risk of HA-BSI associated with SS-NCs versus MV-NCs, nor are there any previously published clinical studies evaluating SS-NCs versus >1 MV-NC. The majority of studies of SS-NCs or MV-NCs have been either in vitro comparisons of microbial ingress after inoculation and repeated activation [18–27] or small single-hospital unit studies that assessed microbial contamination rates in vivo [28] or compared HA-BSI rates between IV systems with 3-way stopcocks versus a single MV-NC [29–31]; two-thirds of these studies found no reduction in the rate of HA-BSIs. Thus, at the time that the most recent CDC IV guideline was written, there were few studies evaluating MV-NC technology [1]. The CDC guideline states that “when the devices are used according to manufacturer’s recommendations, they do not substantially affect the incidence of CR-BSI” [1, p. 13]. Given our data and the SHEA/IDSA compendium, this statement appears to be incorrect. The CDC guideline also recommends “to minimize contamination risk by wiping the access port with an appropriate antiseptic” (category 1B). The specific antiseptic is not indicated, and more-recent data suggest that the most commonly used MV-NC disinfectant (ie, alcohol) may not be effective as commonly used [16] and that 15–30 sec “scrub” of the MV-NC hub with the disinfectant is essential [32] or that chlorhexidine gluconate may be superior to alcohol for MV-NC disinfection [16, 28, 32]. Appropriate MV-NC infection control practices should be derived from more-recent publications and the SHEA/IDSA HA-BSI compendium.

As more negative- or positive-pressure MV-NCs are introduced worldwide, IPs should carefully evaluate their potential impact on patient outcomes before introduction. In many instances, the decision to introduce MV-NCs was made without the input of infection control personnel. Our data illustrate the importance of including infection control personnel in the evaluation of new technologies introduced into health care facilities that may increase HA-BSI risk. Rather than becoming aware of the introduction of new NC technology after the HA-BSI rate has increased, IPs should be partners in evaluating the HCW and patient impact and risk of any new MV-NCs before they are introduced.

Although it may be difficult to definitively establish a causal relationship between MV-NC introduction and increased HA-BSI rates with a study of this type, we do provide strong evidence of this linkage. Four studies that involved smaller populations and took place over shorter periods of time than our own study have found a similar relationship with 2 positive-pressure MV-NCs [9–12]. We have documented an increased HA-BSI risk associated with a variety of different manufacturer’s negative- or positive-pressure MV-NCs. We found a temporal relationship between the introduction of these MV-NCs and an increased HA-BSI rate, as well as a temporal relationship between a decrease in HA-BSI rate and the discontinuation of MV-NC use in favor of a reintroduction of SS-NC use. Our data and other data on contamination of, inadequate disinfection of, and biofilm development on these devices provide supporting biologic plausibility. Furthermore, our data suggest that the SHEA/IDSA recommendations to not routinely use positive-pressure MV-NCs without extensive evaluation should be expanded to include negative-pressure MV-NCs, as well. Hopefully, our data will lead to manufacturers developing safer negative- or positive-pressure MV-NCs that are more resistant to contamination. Until that time, clinicians should closely monitor their NC practices and HA-BSI rates and, if the HA-BSI rate is elevated, examine the potential causative role of MV-NCs.

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