Chlorhexidine Bathing to Reduce Central Venous Catheter-associated Bloodstream Infection: Impact and Sustainability

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ABSTRACT

BACKGROUND: Chlorhexidine bathing has been associated with reductions in healthcare-associated bloodstream infection. To determine the impact and sustainability of the effect of chlorhexidine bathing on central venous catheter-associated bloodstream infection, we performed a prospective, 3-phase, multiple-hospital study.

METHODS: In the medical intensive care unit and the respiratory care unit of a tertiary care hospital and the medical-surgical intensive care units of 4 community hospitals, rates of central venous catheter-associated bloodstream infection were collected prospectively for each period. Pre-intervention (phase 1) patients were bathed with soap and water or nonmedicated bathing cloths; active intervention (phase 2) patients were bathed with 2% chlorhexidine gluconate cloths with the number of baths administered and skin tolerability assessed; post-intervention (phase 3) chlorhexidine bathing was continued but without oversight by research personnel. Central venous catheter-associated bloodstream infection rates were compared over study periods using Poisson regression.

RESULTS: Compared with pre-intervention, during active intervention there were significantly fewer central venous catheter-associated bloodstream infections (6.4/1000 central venous catheter days vs 2.6/1000 central venous catheter days, relative risk, 0.42; 95% confidence interval, 0.25-0.68; P < .001), and this reduction was sustained during post-intervention (2.9/1000 central venous catheter days; relative risk, 0.46; 95% confidence interval, 0.30-0.70; P < .001). During the active intervention period, compliance with chlorhexidine bathing was 82%. Few adverse events were observed.

CONCLUSION: In this multiple-hospital study, chlorhexidine bathing was associated with significant reductions in central venous catheter-associated bloodstream infection, and these reductions were sustained post-intervention when chlorhexidine bathing was unmonitored. Chlorhexidine bathing was well tolerated and is a useful adjunct to reduce central venous catheter-associated bloodstream infection.

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KEYWORDS: Central venous catheter-associated bloodstream infection; Chlorhexidine bathing; Healthcare-associated bloodstream infection.

Reduction of healthcare-associated infections is a top priority for hospitals. In intensive care units, infection is common and associated with significant morbidity and mortality.1 Healthcare-associated infections are often device-
associated and can be caused by antibiotic-resistant pathogens that flourish in the hospital environment. Preventing healthcare-associated infections requires rigorous infection control efforts that are usually focused on the healthcare provider.\(^7\) A complementary infection control measure is to reduce the number of patients colonized with a hospital pathogen through decolonization strategies. This is known as “source control,” but its use has been limited by few available modalities.

Bathing patients with the antiseptic chlorhexidine is a potential tool for source control. The mechanism of antibacterial action involves attachment of the positively charged chlorhexidine to the negatively charged bacterial cell causing leakage of cytoplasm, resulting in bactericidal or bacteriostatic activity. Chlorhexidine reduces both resident and transient skin flora with a residual effect that lasts at least 6 hours.\(^3,4\)

Vernon et al\(^5\) demonstrated that cleansing medical intensive care unit patients with 2% chlorhexidine-saturated cloths resulted in significantly fewer colonies of vancomycin-resistant enterococci on patients’ skin and significantly less contamination of the environment and healthcare workers’ hands. The incidence of acquisition of vancomycin-resistant enterococci was reduced by 60%.\(^5\) Subsequently, studies of chlorhexidine bathing in the same unit and in another medical intensive care unit found that the period of chlorhexidine bathing was associated with significant reductions in primary bloodstream infections\(^6\) and central venous catheter-associated bloodstream infections.\(^7\) By using an alternative method to the chlorhexidine saturated cloths, Climo et al\(^8\) evaluated the effect of adding 4% liquid chlorhexidine to patients’ bath water. In that multiple-hospital study, there were significantly fewer vancomycin-resistant enterococcal bloodstream infections and fewer patients acquired vancomycin-resistant enterococci and methicillin-resistant Staphylococcus aureus during the period of chlorhexidine bathing.

To extend our understanding of the efficacy of chlorhexidine bathing, we performed a prospective, 3-phase, multiple-hospital study designed to evaluate the effect of chlorhexidine bathing on central venous catheter-associated bloodstream infection and the sustainability of any effect detected. In addition, skin tolerability and frequency of bathing were assessed during the active intervention period.

### MATERIALS AND METHODS

#### Study Design, End Points, and Setting

The study was a prospective, 3-phase study performed from April 1, 2008, to August 31, 2010. This study was performed at 1 tertiary care hospital and 4 community hospitals in Westchester County, New York. The study units were the medical intensive care unit of the tertiary care hospital, which houses oncology and critically ill medical patients but does not include trauma/surgical patients; the respiratory care unit of the tertiary care hospital, which houses medical and surgical patients requiring ongoing mechanical ventilation or respiratory care; and medical-surgical intensive care units of the 4 community hospitals, each of which houses a variety of critically ill medical and surgical patients.

The study end point was hospital-acquired central venous catheter-associated bloodstream infection rates. The inclusion criterion for chlorhexidine bathing was admission to the study unit. Exclusion criteria were pregnancy, breast feeding, chlorhexidine allergy, and severely denuded skin. The study was approved with a waiver for written informed consent by the New York Medical College Committee for Protection of Human Subjects and by the institutional review board of each hospital.

Phase 1 (pre-intervention) started April 1, 2008, at all hospitals and lasted for 6 to 9 months on each unit; the different time intervals allowed units to transition to phase 2 separately. During phase 1, patients were bathed according to hospital protocol; nonmedicated bathing cloths were used at sites A, B, and E, and soap and water in a basin bath were used at sites C, D, and F.

Phase 2 (active intervention) began immediately after phase 1 and lasted for 8 months on each unit. During phase 2, bathing was performed with 2% chlorhexidine gluconate cloths (Sage Products Inc, Cary, Ill) provided to the hospital at no charge. The bathing protocol was to use 1 package of 6 cloths with 1 cloth for each of the following anatomic areas: the neck/shoulders and chest, both arms and hands, abdomen/groin/perineum, right leg/foot, left leg/foot, and back and buttocks. If needed, more than 1 package was used. The face was cleansed with nonmedicated cloths. During the week before chlorhexidine bathing began, all nursing staff received in-service education on bathing procedures, study requirements to record the chlorhexidine baths administered on a research flow sheet, and how to assess skin tolerability (at each shift) in consultation with research personnel. Research personnel made rounds on all study units at least weekly.

Phase 3 (post-intervention) began immediately after phase 2 and lasted for 12 months on each unit. During phase 3 hospitals could continue chlorhexidine bathing, but the product was no longer supplied by the study. All 6 units
chose to continue chlorhexidine bathing using the same product and bathing protocol. Research personnel kept track of whether chlorhexidine bathing was in use, but the baths administered were no longer recorded on research forms. Research personnel continued to be available for any questions regarding skin tolerability.

Throughout all phases of the study, the Infection Prevention and Control Department at each site had policies and procedures in the intensive care unit that emphasized the importance of insertion checklists to reduce central venous catheter-associated bloodstream infection.

During the pre-intervention period of the study, site C began using an antibiotic impregnated central venous catheter 5 months before chlorhexidine bathing began, and site D began using a chlorhexidine-impregnated central venous catheter dressing 3 months before chlorhexidine bathing began.

Definitions

All positive blood cultures were reviewed by infection prevention and control staff at each site and classified as central venous catheter-associated bloodstream infection and as hospital-acquired using the National Healthcare Safety Network of the Centers for Disease Control and Prevention definition. A central venous catheter-associated bloodstream infection was defined as a patient with a central venous catheter in place with a recognized pathogen cultured from one or more blood cultures AND the organism was not related to an infection at another site; or a common skin organism was cultured from 2 or more blood cultures drawn on separate occasions (within 2 days of each other) AND at least 1 of the following signs or symptoms was present: fever (>38°C), chills, or hypotension, AND the signs and symptoms and positive blood cultures were not due to infection at another site. Central venous catheter-associated bloodstream infection was defined as acquired on the study unit if the signs and symptoms of infection were not incubating at the time of admission and the positive blood culture was drawn while the patient was housed on the unit or within 48 hours of the time of discharge from the unit. The denominator for the central venous catheter-associated bloodstream infection rates was 1000 central venous catheter days. Days eligible for a bath included the day of admission to the unit, the day of discharge from the unit, and all days hospitalized on the unit.

Statistical Methods

The sample size estimate was derived from a known rate of 4 healthcare-associated bacteremias per 1000 patient days at the tertiary care medical center during the year before the study began. On the basis of published studies, it was assumed that chlorhexidine bathing would result in a 50% reduction of healthcare-associated bloodstream infection.

To achieve a statistically significant reduction ($P = .05$) in central venous catheter-associated bloodstream infection with a power of 80%, the sample size estimate was 12,700 patient days each for the pre-intervention period and 12,700 patient days for the active intervention period.

Infection rates were modeled over the 3 study periods using Poisson regression. In this approach, total infection counts are adjusted for total central venous catheter days, stratified by hospital and study period. Both hospital and study period were modeled using indicator variables. Results are expressed as adjusted incidence rate ratios with accompanying 95% confidence intervals (CIs). Pairwise comparison of rates over study periods was conducted using the Wald test with Bonferroni’s adjustment to the $P$ value. We conducted a subanalysis that excluded the 2 sites (C and D) that had initiated parallel interventions that may have influenced study results. The subanalyses were conducted as described above. Analyses were conducted using Stata version 11.1 (StataCorp, College Station, Tex) and SAS version 9.1 (SAS Institute Inc, Cary, NC). A critical test level of 5% was considered statistically significant, unless adjusted for multiple comparisons.

RESULTS

The study unit characteristics, number of beds, and average length of stay during each period of the study are shown in Table 1. The number of patient days and the number of admissions for each study phase was 12,603 patient days, 1808 admissions for the pre-intervention period; 13,864 patient days, 1832 admissions for the active intervention period; and 19,914 patient days and 2834 admissions for the

<table>
<thead>
<tr>
<th>Unit No. of Beds</th>
<th>Unit Type</th>
<th>Average Length of Stay in Days*</th>
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<tr>
<td></td>
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<td>Pre-Intervention</td>
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<tr>
<td>B 20</td>
<td>Respiratory care</td>
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<tr>
<td>C 12</td>
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<tr>
<td>F 12</td>
<td>Medical surgical intensive care</td>
<td>7.3</td>
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</tbody>
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*Derived from the number of patient days divided by the number of admissions.
†On the first day of the active intervention period, the unit moved from a 7-bed unit to an 11-bed unit.
post-intervention period. On the first day of the active intervention period, site A moved the intensive care unit from a 7-bed unit to a new 11-bed unit. Exclusions from chlorhexidine bathing occurred for 2 patients during the active intervention period, 1 due to pregnancy and 1 due to Stevens-Johnson syndrome. Chlorhexidine bathing was discontinued in 3 patients because of skin rash and restarted in 2 of the 3 patients without adverse event; the third patient also had thrombocytopenia that resolved with the discontinuation of multiple medications and chlorhexidine.

During the active intervention period, chlorhexidine baths were given on 12,196 (82%) of 14,942 days that patients were eligible for a bath. A total of 18,357 chlorhexidine baths were given, indicating an average of 1.5 chlorhexidine baths daily. The reasons recorded for not administering a chlorhexidine bath included the patient being admitted to or discharged from the unit that day (54% of missed baths) or unknown (46% of missed baths). During the post-intervention period, chlorhexidine baths were in use by study units for 17,519 (88%) of 19,914 post-intervention study days. Two units, E and F, did not use chlorhexidine for bathing for 4 and 5 months, respectively, because of lapses in product supply at the beginning of the post-intervention period when chlorhexidine baths were no longer provided by the study.

Rates of central venous catheter-associated bloodstream infection, unadjusted and adjusted for study center, are shown in Table 2. Compared with the pre-intervention period adjusted rate (6.4/1000 central venous catheter days; relative risk [RR], 0.42; 95% CI, 0.25-0.68; P < .001) (Table 2). This reduction was sustained during the post-intervention period (2.9/1000 central venous catheter days; RR, 0.46; 95% CI, 0.30-0.70; P < .001) (Figure 1). There was little difference in the rates of central venous catheter-associated bloodstream infection between the active intervention period and the post-intervention period (P = .9). During the lapse in chlorhexidine bath supply at sites E and F during the post-intervention period, 1 site had 2 infections (Table 2). These numbers were considered too small to reassess the chlorhexidine effect. A subanalysis was performed excluding sites C and D, which had begun using other products that may reduce central venous catheter-

![Figure 1](image)

**Figure 1** Adjusted rates of central venous catheter-associated bloodstream infection with limits of the 95% CI range for each point estimate.
associated bloodstream infection during the pre-intervention period. By excluding sites C and D, compared with the pre-intervention rate (2.5/1000 central venous catheter days), there was still a significant reduction in the rate of central venous catheter-associated bloodstream infection during the active intervention period (1.3/1000 central venous catheter days; RR, 0.54; 95% CI, 0.33-0.90; \( P < .005 \)), and this reduction was sustained during the post-intervention period (1.2/1000 central venous catheter days; RR, 0.49; 95% CI, 0.31-0.78; \( P < .003 \)).

The relative frequency of specific central venous catheter types in use at the time of infection was as follows: pre-intervention: peripherally inserted central catheter 46%, triple lumen catheter 50%, hemodialysis catheter plus a triple lumen catheter or peripherally inserted central catheter 2%, hemodialysis catheter alone 2%; active intervention period: peripherally inserted central catheter 40%, triple lumen catheter 32%, hemodialysis catheter plus a triple lumen catheter or peripherally inserted central catheter 24%, subcutaneous venous access device 4%; post-intervention period: peripherally inserted central catheter 35%, triple lumen catheter 28%, hemodialysis catheter plus a triple lumen catheter or peripherally inserted central catheter 31%, hemodialysis catheter alone 3%, subcutaneous venous access device 5%.

During the pre-intervention period, the number of central venous catheter-associated bloodstream infections in which gram-positive bacteria were recovered decreased from 21 to 15, with no reduction in the number of infections involving enterococci, including vancomycin-resistant enterococci. Of note, during the active intervention period central venous catheter-associated bloodstream infection due to vancomycin-resistant enterococci occurred predominantly in severely neutropenic oncology patients and severely immunosuppressed patients housed in a single unit, whereas pre-intervention the cases of vancomycin-resistant enterococci causing central venous catheter-associated bloodstream infection were dispersed throughout several units.

### DISCUSSION

In this prospective, multiple-hospital study, there was a significant reduction in central venous catheter-associated bloodstream infection during the active intervention period in which chlorhexidine bathing was used, compared with pre-intervention when patients were bathed with soap and water or nonmedicated bathing cloths. This reduction was sustained during the 1 year post-intervention period during which chlorhexidine bathing was continued for 88% of the time and there was no direct supervision by study staff. The reduction in central venous catheter-associated bloodstream infection was presumably due to less patient skin colonization with hospital pathogens, resulting in fewer opportunities for central venous catheter contamination, colonization, and subsequent bacteremia. We quantified the number of chlorhexidine baths given and found that patients often received more than 1 bath per day. Compliance with chlorhexidine bathing was high, and chlorhexidine bathing was well tolerated.

This study adds to the developing body of evidence associating chlorhexidine bathing with reductions in health-
care-associated bacteremia. Our study is the first prospective, multiple-hospital study evaluating the use of chlorhexidine bathing as a measure to reduce central venous catheter-associated bloodstream infection. It also is the first study to include a post-intervention period as part of the prospective study. In contrast with the active intervention period when baths administered were recorded on a research flow sheet, during the post-intervention period this was no longer done to allow for a more “real-life” situation. The sustainability of central venous catheter-associated bloodstream infection rate reductions post-intervention lends support to the concept that the infection reduction was related to the use of chlorhexidine bathing; however, we cannot exclude improved or more frequent bathing overall as the principal factor. When the units that had initiated other measures to reduce central venous catheter-associated bloodstream infection were excluded, the subanalysis still demonstrated significant reductions in central venous catheter-associated bloodstream infection rates during both the active intervention and the post-intervention periods.

Studies of chlorhexidine bathing have been limited by the before and after study design. One study, however, used a stronger cross-over study design in which there was a simultaneous control in which 2 sides of a medical intensive care unit alternated between chlorhexidine bathing and nonmedicated bathing. In this study, Bleasdale et al found significantly fewer primary bloodstream infections during the period of chlorhexidine bathing, and these infections were mostly central venous catheter-associated. The bloodstream infections were primarily due to coagulase-negative staphylococci and enterococci. The only study involving more than a few central venous catheter-associated bloodstream infections due to gram-negative bacteria was performed at a long-term acute care hospital where 19 (32%) of the infections pre-intervention involved gram-negative bacteria. As in our study, these gram-negative central venous catheter-associated bloodstream infections were reduced during chlorhexidine bathing, as were central venous catheter-associated bloodstream infections due to coagulase-negative staphylococci.

The respiratory care unit patients in our study had the highest rate of central venous catheter-associated bloodstream infection during the pre-intervention period and the greatest reduction in central venous catheter-associated bloodstream infection (Table 2). Characteristics specific to respiratory care patients could affect central venous catheter-associated bloodstream infection. For example, tracheostomy can be a risk factor for central venous catheter-associated bloodstream infection, particularly when the central venous catheter is located in the internal jugular vein in close proximity to tracheal secretions, and mechanical ventilation alone has been associated with central venous catheter-associated bloodstream infection. We did not attempt to study these factors prospectively during the study, but subsequently reviewed data for the unit. Although the percentage of patients receiving mechanical ventilation was the same for the pre-intervention and active intervention periods, the percentage of patients with tracheostomy was significantly greater ($P < .01$) during the active intervention period. One could speculate that the reduction of central venous catheter-associated bloodstream infection on this unit might have been even larger if the percentage of patients with tracheostomies had been similar.

Although we did not attempt to formally study the cost benefit of chlorhexidine bathing, given an attributable cost estimate of $45,000 per central venous catheter-associated bloodstream infection, the cost of chlorhexidine bathing is easily outweighed by the savings from preventing a few central venous catheter-associated bloodstream infections. By using the bathing data collected from the active intervention period, had the hospitals paid for the chlorhexidine baths, there would have been a $4.10 per bath higher cost for the hospitals that switched to chlorhexidine-impregnated cloths from nonmedicated bathing cloths, and a $4.94 to $5.10 per bath increased cost for the hospitals that switched to chlorhexidine-impregnated cloths from soap and water, resulting in an overall increased expenditure ranging from $79,867 to $81,006. There were 21 fewer central venous catheter-associated bloodstream infections during the active intervention period compared with the pre-intervention period. This would be equivalent to a savings of $945,000, which is more than 10 times the cost of chlorhexidine bathing. Nursing staff also found the baths easy to administer and preferable to soap and water in a basin.

Limitations

The limitations of this study are the lack of patient-specific data and severity of illness data to determine whether the patient population changed between periods. The need for patient-specific data is apparent as discussed above regarding the respiratory care patients, and others have found discrepant results in different populations. For example, Popovich et al found no reduction in central venous catheter-associated bloodstream infection during chlorhexidine bathing of surgical intensive care unit patients, whereas medical intensive care unit patients at the same hospital had significant reductions in central venous catheter-associated bloodstream infection with chlorhexidine bathing. In addition, it might have been useful to have the denominator of central venous catheter days stratified by central venous catheter type to uncover patient population or practice changes for the study periods. This was not done because such a stratification is substantially more labor-intensive. Our study was not a randomized double-blind trial, and thus we cannot fully exclude confounding variables. Any bias on the interpretation of bacteremia as central venous catheter-associated during the different study periods should have been minimized because central venous catheter-associated bloodstream infection was publicly reported during the timeframe of this study and application of the National Healthcare Safety Network definition of this infection was monitored by the New York State Department of Health.
**CONCLUSIONS**

In the 2011 Guidelines for the Prevention of Intravascular Catheter-Related Infections by the Centers for Disease Control and Prevention, daily cleansing with 2% chlorhexidine was given a category II recommendation, which means it is supported by suggestive clinical or epidemiologic studies. Our multiple-hospital, 3-phase study demonstrates that chlorhexidine bathing is a simple, well-tolerated infection control intervention that seems to significantly reduce central venous catheter-associated bloodstream infection in intensive care unit/respiratory care unit settings. Chlorhexidine bathing is likely to be an important adjunctive infection control measure for the prevention of central venous catheter-associated bloodstream infection.

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**References**


