Effectiveness of Chlorhexidine Bathing to Reduce Catheter-Associated Bloodstream Infections in Medical Intensive Care Unit Patients

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Objective: To determine whether patients bathed daily with chlorhexidine gluconate (CHG) have a lower incidence of primary bloodstream infections (BSIs) compared with patients bathed with soap and water.

Methods: The study design was a 52-week, 2-arm, crossover (ie, concurrent control group) clinical trial with intention-to-treat analysis. The study setting was the 22-bed medical intensive care unit (MICU), which comprises 2 geographically separate, similar 11-bed units, of the John H. Stroger Jr (Cook County) Hospital, a 464-bed public teaching hospital in Chicago, Illinois. The study population comprised 836 MICU patients. During the first of 2 study periods (28 weeks), 1 hospital unit was randomly selected to serve as the intervention unit in which patients were bathed daily with 2% CHG-impregnated washcloths (Sage 2% CHG cloths; Sage Products Inc, Cary, Illinois); patients in the concurrent control unit were bathed daily with soap and water. After a 2-week washout period at the end of the first period, cleansing methods were crossed over for 24 more weeks. Main outcome measures included incidences of primary BSIs and clinical (culture-negative) sepsis (primary outcomes) and incidences of other infections (secondary outcomes).

Results: Patients in the CHG intervention arm were significantly less likely to acquire a primary BSI (4.1 vs 10.4 infections per 1000 patient days; incidence difference, 6.3 [95% confidence interval, 1.2-11.0). The incidences of other infections, including clinical sepsis, were similar between the units. Protection against primary BSI by CHG cleansing was apparent after 5 or more days in the MICU.

Conclusions: Daily cleansing of MICU patients with CHG-impregnated cloths is a simple, effective strategy to decrease the rate of primary BSIs.

Trial Registration: clinicaltrials.gov Identifier: NCT00130221

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Each year, an estimated 80,000 patients in US intensive care units (ICUs) incur catheter-associated bloodstream infections (BSIs). Because of the impact on patient outcomes and since many of these infections are preventable, reduction in BSI risk is the focus of several recent or ongoing patient safety initiatives.1-5

Most catheter-associated BSIs result from contamination of the catheter by bacteria residing on patients' skin at the time of device insertion, later from microorganisms migrating from the skin to catheter tip,6 or after catheter hub contamination, often also by patients' own skin flora. The risk of BSI is reduced by antiseptic skin preparation immediately before catheter insertion and by keeping microbial density at the insertion site low while the catheter is in place.6,7 Chlorhexidine gluconate (CHG), which has broad antimicrobial activity, prolonged residual effect, and superiority over iodophor skin preparations, is the recommended agent for disinfecting skin before catheter insertion.7-10

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Because catheter-associated BSI is usually caused by patients' resident skin flora, decolonization of a larger area of skin has biological plausibility for reducing catheter-associated infection rates. In a previous study with historical controls,11 we found that compared with soap and water bathing, daily bathing with CHG reduced microbial density on patients' skin, incidence of vancomycin-resistant enterococcal colonization, and BSI rates.1,12 In the present study, we report a new clinical trial using concurrent controls and a crossover design to test whether CHG cleansing would decrease the incidence of primary BSIs compared with soap and water baths.
We studied the medical ICU (MICU) at John H. Stroger Jr (Cook County) Hospital, a 464-bed public teaching hospital in Chicago, Illinois. The 22-bed MICU comprises 2 geographically separate, similar 11-bed units. Each unit has a dedicated nursing staff; 1 team of attending and resident physicians cares for patients in both units. The MICU catheter insertion policy mandated sterile technique, full barrier drapes, and insertion site disinfection with 2% CHG; antiseptic- or antibiotic-coated catheters were not used. No other catheter-associated BSI infection control interventions were implemented during the study.

We calculated a sample size to detect a 75% reduction of primary BSI risk, a reduction consistent with results of our earlier study. Using previously collected data, we estimated MICU census of 235 patient-days per unit per month and a primary BSI rate of 12 per 1000 patient-days. Setting the α level at .05 and power at 80%, we calculated a prespecified study duration of 12 months.

INTERVENTION

Crossover

We divided the study into 2 periods. During the first, June 8 through December 20, 2005 (28 weeks), we randomly selected one unit (MICU A) to serve as the intervention unit where patients were bathed daily with 2% CHG–impregnated washcloths (Sage); this was designated the CHG arm. Patients in the concurrent control unit were bathed daily with soap and water. The first period was followed by a 2-week “washout” period during which patients were bathed with soap and water in both units. We then crossed over the patient cleansing procedures during the second 24-week period.

DESIGN OVERVIEW

This was a prospective, 2-arm, crossover (ie, concurrent control group) clinical trial of daily bathing with no-rinse, 2% CHG-impregnated washcloths (Sage 2% chlorhexidine gluconate impregnated washcloths; Sage Products Inc, Cary, Illinois) vs soap and water bathing. The main study outcomes were primary BSI and clinical (culture-negative) sepsis; the secondary study outcome was the occurrence of other nosocomial infections. The institutional review board waived the need for informed consent.

SETTING AND PARTICIPANTS

We studied the medical ICU (MICU) at John H. Stroger Jr (Cook County) Hospital, a 464-bed public teaching hospital in Chicago, Illinois. The 22-bed MICU comprises 2 geographically separate, similar 11-bed units. Each unit has a dedicated nursing staff; 1 team of attending and resident physicians cares for patients in both units. The MICU catheter insertion policy mandated sterile technique, full barrier drapes, and insertion site disinfection with 2% CHG; antiseptic- or antibiotic-coated catheters were not used. No other catheter-associated BSI infection control interventions were implemented during the study.

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Bathing Procedure

Nurses were instructed on the standardized bathing procedure relevant to their unit as described previously, with the following modifications. For CHG baths, 8 cloths, rather than 6, were used to clean patients’ bodies up to the jawline, and 2 nomedicated cloths were used to clean patients’ faces. For patient comfort, packaged cloths were placed in a dedicated warmer (51.7°C) before use. For soap and water baths, nurses used warm water in a disposable basin and bar soap (Pure & Natural; Dial Corp, Scottsdale, Arizona) applied with 10 fresh terrycloth washcloths per bath. We monitored nurses’ bathing technique in both arms episodically.

All patients were bathed using the unit’s designated procedure with the following exceptions. Patients in the CHG arm with greater than 20% body surface area disruption of skin integrity, who declined participation or who developed a rash that might be attributed to CHG, were bathed with soap and water.

Data Collection

For all patients, we recorded age, sex, invasive device use (ie, intravascular devices, urinary bladder catheters, mechanical ventilation, and feeding tubes), daily temperature, decubitus ulcers, hemodialysis, vasopressor and antibiotic receipt, APACHE II (Acute Physiology and Chronic Health Evaluation II) score, immunosuppressive conditions (human immunodeficiency virus, diabetes, neutropenia, leukemia, and lymphoma), and in-unit mortality.

For infection surveillance, daily electronic review of microbiological cultures and new orders for antibiotic therapy were obtained for participants who were present in the MICU for more than 48 hours. To determine whether a patient had an infection related to MICU stay, we performed a medical record review whenever a positive clinical culture was detected or a new order for antibiotic therapy was given. Clinical and laboratory data were entered on standardized forms and evaluated independently by 3 physician investigators (S.B., I.G., and R.W.). The initial 2 reviewers (S.B. and I.G.) were unblinded to intervention assignment; the third reviewer (R.W.) was blinded. Discrepant interpretations were adjudicated by discussion and consensus among the 3 reviewers; if uncertainties persisted, a fourth physician investigator (W.T.), also blinded to intervention assignment, was consulted. To evaluate whether reviews were biased, we also calculated BSI rates using a computer algorithm on a data warehouse. Agreement between investigator reviews and computer algorithm determinations was high (κ = 0.74), the same as observed in a previous study. Also, there was no difference in level of agreement between arms (P = .82), suggesting that misclassification bias during BSI determination was rare or nonexistent.

Events prompting medical record review were categorized as noninfectious, infection related to MICU stay, or infection present or incubating before MICU admission. Using Centers for Disease Control and Prevention definitions, we classified infections that were determined to be related to MICU stay as primary BSI (intravascular catheter-associated, laboratory-confirmed BSI), clinical (culture-negative) sepsis (fever with no apparent infectious source that was treated with antibiotics), secondary BSI (related to another clinical site), ventilator-associated pneumonia, pneumonia, urinary tract infection, Clos-
treatment for continuous variables and categorical variables using the Wilcoxon rank-sum test or the t test for each arm. We included an interaction term. We also compared the incidence difference for central venous catheter-associated primary BSIs per 1000 central line-days (days a patient had a central venous catheter). To evaluate and adjust for potential confounders, we constructed multivariable Poisson regression models. We reported the results of a final multivariate model that included the strongest independent predictors of primary BSI. To test the association between geographic unit and patient bathing method, we included an interaction term. In addition to comparing soap and water with CHG bathing, we evaluated other potential predictors (eg, invasive device use) of primary BSI using Poisson regression.

We graphically compared occurrences of primary BSI or mortality over time between study arms by constructing separate Kaplan-Meier plots; we calculated log-rank test statistics for each curve. For construction of the Kaplan-Meier curve for primary BSI occurrence and calculation of log-rank test statistic, we included only a patient’s first BSI. We present the hazard rate for mortality after adjusting for severity of illness (APACHE II score) using Cox proportional hazards models. We calculated antibiotic use for each arm as proportion of days that a patient received an antimicrobial agent and number of new antibiotic prescriptions (ie, ≥3 days between antibiotic transactions) per 100 patient-days.

We compared patient characteristics between CHG and soap and water arms using the Wilcoxon rank-sum test or the t test for continuous variables and χ² test for categorical variables. All statistical analyses were done using Stata version 9.2, (StataCorp, College Station, Texas).

RESULTS

There were 391 patient admissions (2210 patient-days) in the CHG arm and 445 patient admissions (2119 patient-days) in the soap and water arm; the differences reflect longer length of stay in the CHG arm (5.7 days vs 4.8 days; P=.06). The mean patient age was 52 years, most patients were men, and the 2 groups were similar (Table 1). The number and percentage of days a patient had a central venous catheter was higher in the CHG arm (1399 [63%] vs 1248 [59%]). Three subjects were excluded from the CHG arm after developing rashes that were ultimately determined not to be due to CHG.

We identified 31 primary BSIs in 27 patients. Patients in the CHG arm were significantly (61%) less likely to acquire a primary BSI; the incidence of other infections was similar between study arms (Table 2). For the combined outcome of primary BSI and culture-negative sepsis, there were less occurrences in the CHG arm, but the difference was not statistically significant (15 vs 11 per 1000 patient-days; P=.34). Protection against primary BSI by CHG cleansing was apparent 5 or more days after admission to the MICU (Figure 2).

Using central line-days as the denominator, we again found that patients in the CHG arm were at lower risk of primary catheter-associated BSI compared with patients bathed with soap and water (6.4 vs 16.8 BSIs per 1000 central line-days; P=.01). After adjusting for invasive device use (ie, ventilator-days or urinary bladder catheter-days), the 2 study arms had similar incidences of...
ventilator-associated pneumonia and urinary tract infection (data not shown).

By bivariable analysis, predictors of primary BSI included soap and water bathing; mechanical ventilation; and presence of femoral or internal jugular, but not subclavian, catheters. By multivariable analysis, after adjusting for placement of a femoral central venous catheter, mechanical ventilation, and geographic unit, soap and water bathing remained an independent predictor for occurrence of primary BSI (Table 3).

When we analyzed distribution of clinical isolates, we found a significantly higher incidence of urine isolates from patients in the soap and water arm (13 per 1000 patient-days vs 7 per 1000 patient-days; P = .05). Although not statistically significant, there was also a higher incidence of isolates from blood cultures in the soap and water arm (24 per 1000 patient-days vs 17 per 1000 patient-days; P = .11). Regardless of clinical source, CHG bathing reduced the incidence of gram-positive bacterial isolates; recovery of isolates from other microbial categories (ie, yeasts, molds, and gram-negative bacteria) was similar between study arms. There was a single methicillin-resistant *Staphylococcus aureus* primary BSI, which occurred in the soap and water arm.

We also evaluated in-unit mortality and antimicrobial use. Earlier mortality among patients in the soap and water arm may have been due to chance (P = .23). After adjusting for APACHE II score, the earlier mortality was less likely due to chance (hazard ratio, 1.4; 95% confidence interval, 0.9-2.1; P = .12) (Figure 3). There was a nonsignificant trend toward more new antimicrobial prescriptions per 100 patient-days in the soap and water arm compared with the CHG arm (16 vs 14; P = .07); however, the proportion of days patients received antibiotics was similar (0.76 vs 0.79; P = .37).

Of 64 blood isolates, 57 (89%) were available for CHG susceptibility testing. The median CHG minimum inhibitory concentration was slightly higher for isolates identified in the CHG arm compared with those in the soap and water arm (2 µg/mL [interquartile range, 1.4-4 µg/mL] vs 1 µg/mL [interquartile range, 0.5-2 µg/mL]; P = .06). This was owing to the less frequent recovery of highly CHG-susceptible, gram-positive bacteria in the CHG arm (eg, as shown for primary BSI isolates; Table 4) rather than to an increase in the absolute number of isolates with elevated CHG minimum inhibitory concentrations.

In a 12-month clinical trial with a concurrent control group, bathing MICU patients daily with no-rinse, 2% CHG-impregnated cloths resulted in a 61% relative decline in incidence of primary BSIs. This reduction was comparable to or better than reductions in primary BSIs achieved in 3 recent multicenter cohort studies of ICU patients who received bundled evidence-based interventions. In contrast to those investigations, we reduced the primary BSI rate by improving a required, routine patient care activity (ie, patient bathing) without introducing additional actions.

Our findings extend the work of others who have reported that skin antisepsis with CHG before device insertion reduces intravascular device–associated infections by reducing bacterial skin burden and that maintaining a low density of bacterial skin colonization at the catheter insertion site through the use of CHG-impregnated dressings while a catheter is in place provides added benefit. Compared with soap and water

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**Table 2. Comparison of Incidence of Infection by Method of Bathing Patients and Infection Category**

<table>
<thead>
<tr>
<th>Infection Category</th>
<th>Soap and Water</th>
<th>2% CHG</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary BSI</td>
<td>22</td>
<td>9</td>
<td>13.3 (1.2 to 11)</td>
<td>.01</td>
</tr>
<tr>
<td>Contaminant</td>
<td>9</td>
<td>4</td>
<td>5.0 (.9 to 5.7)</td>
<td>.16</td>
</tr>
<tr>
<td>Clinical sepsis</td>
<td>9</td>
<td>4</td>
<td>-5.0 (-7.5 to 1.5)</td>
<td>.20</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>17</td>
<td>13</td>
<td>4.0 (-2.3 to 7.1)</td>
<td>.41</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia</td>
<td>15</td>
<td>18</td>
<td>-3.0 (-6.3 to 4.1)</td>
<td>.69</td>
</tr>
<tr>
<td>Secondary BSI</td>
<td>5</td>
<td>5</td>
<td>0.0 (-2.8 to 3.0)</td>
<td>.96</td>
</tr>
<tr>
<td><em>Clostridium difficile</em> diarrhea</td>
<td>20</td>
<td>21</td>
<td>1.0 (-5.9 to 5.7)</td>
<td>.98</td>
</tr>
</tbody>
</table>

Abbreviations: BSI, bloodstream infection; CHG, chlorhexidine gluconate; CI, confidence interval.

<table>
<thead>
<tr>
<th>Study arm</th>
<th>Soap and Water</th>
<th>2% CHG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of Patients Without BSI</td>
<td>P = .04</td>
<td></td>
</tr>
</tbody>
</table>

**COMMENT**

In a 12-month clinical trial with a concurrent control group, bathing MICU patients daily with no-rinse, 2% CHG-impregnated cloths resulted in a 61% relative decline in incidence of primary BSIs. This reduction was comparable to or better than reductions in primary BSIs achieved in 3 recent multicenter cohort studies of ICU patients who received bundled evidence-based interventions. In contrast to those investigations, we reduced the primary BSI rate by improving a required, routine patient care activity (ie, patient bathing) without introducing additional actions.

Our findings extend the work of others who have reported that skin antisepsis with CHG before device insertion reduces intravascular device–associated infections by reducing bacterial skin burden and that maintaining a low density of bacterial skin colonization at the catheter insertion site through the use of CHG-impregnated dressings while a catheter is in place provides added benefit. Compared with soap and water
bathing, CHG cleansing results in a persistent several log_{10} reduction in density of microbial skin colonization. Thus, daily bathing with CHG ensures that most patients will have relatively low baseline bacterial skin burden, which would compensate partially for deficiencies in skin antisepsis and minimize inadvertent contamination of the central venous catheter or related equipment during catheter insertion. Further, after the catheter is inserted, the reduced microbial load may decrease risk of contamination of health care workers’ hands, catheter insertion sites, and catheter hubs. Based on our findings (Figure 2), these risks may manifest clinically 5 or more days after MICU admission.

In contrast to the dramatic decline in primary bacteremias in the CHG arm, we detected a nonsignificant increase in the rate of clinical sepsis among patients bathed with CHG-impregnated cloths. This may have resulted from a decreased likelihood of positive blood cultures in syndromes that otherwise would have been categorized...
as contaminated blood cultures or primary BSIs. Alternatively, it may have been a function of application of a nonspecific designation (ie, clinical sepsis) to a constellation of signs and symptoms often due to noninfectious causes in critically ill patients.\textsuperscript{21,22}

Compared with the decline in primary bacteremias, the difference in incidence of contaminated blood cultures between the CHG and soap and water arms was of smaller magnitude and may have been due to chance. Alternatively, our sample may not have been large enough to identify a statistically significant reduction. A diminution in blood culture contamination rate is clinically relevant because many patients are treated for infection despite the low likelihood of true BSI; unnecessary treatment exposes patients to antibiotics and may increase the length of stay and costs.\textsuperscript{23}

We had hypothesized that CHG, in addition to decreasing incidence of primary BSIs, would reduce urinary tract infection rates by lessening periurethral microbial density. Although there was a significant decline in number of urinary isolates in the CHG arm, incidence of urinary infection was unchanged. These findings are consistent with those of previous studies that failed to demonstrate reductions in bacteruria after intensified urocare.\textsuperscript{24}

We detected a trend toward delayed ICU mortality in the CHG arm; this was not statistically significant, perhaps because we focused on primary BSI for sample size calculations. We did not collect data on 30-day mortality. There was a nonsignificant trend toward fewer antibiotic courses in the CHG arm, although the relative proportion of antibiotic use to treat primary BSIs was not enough to have an impact on total antibiotic consumption.

A frequent concern about increased use of antiseptics is the development of microbial resistance. Blood culture isolates recovered from patients in the CHG arm had slightly higher CHG minimum inhibitory concentrations than did isolates recovered from patients in the soap and water arm. However, this was owing to a reduction in BSI incidence by isolates that typically are inhibited by very low CHG concentrations, such as coagulase-negative staphylococci, rather than by an increase in the number of microorganisms with decreased CHG susceptibility.

Strengths of our study include use of a concurrent control group, crossover design, intention-to-treat analysis, large number of patient-days, and comprehensive capture of infection events by dual manual and electronic surveillance. Our study also has several limitations. The nursing staff could not be blinded to the intervention. Only 1 of 3 physician investigators who categorized BSIs and the category adjudicator were blinded to study arm designation, which could have resulted in bias in classification of primary BSIs. The absence of an increase in secondary BSIs or blood culture contaminants in the CHG arm and the strong agreement between human reviewers and a computer algorithm in the categorization of BSIs argue against misclassification. The CHG arm had fewer patients but equivalent patient-days, which reflected a slightly longer length of stay. Since BSI risk increases during a patient’s ICU stay, the longer stay in the CHG arm actually may have biased against finding a protective effect from CHG cleansing. We performed the study in a single center with a baseline rate of primary BSI higher than rates reported to a national surveillance system\textsuperscript{25} but lower than those reported during a study in MICUs at other academic centers.\textsuperscript{5} Although our results may not be applicable to all ICUs, the reduced incidence of catheter-associated BSIs in the CHG arm was greater than that observed in all 5 MICUs enrolled in a recent multicenter study of bundled, evidence-based measures to reduce catheter-associated BSI.\textsuperscript{3} Finally, the soap and water arm had a disproportionate number of primary BSIs caused by coagulase-negative staphylococci. Although coagulase-negative staphylococci may be less virulent than other microbial species, their recovery results in preventable vancomycin use and can be associated with substantial morbidity and mortality.\textsuperscript{26}

Daily cleansing of MICU patients with CHG-impregnated cloths is a simple and effective strategy to decrease the rate of primary BSIs. We believe this approach is a useful adjunctive infection control measure.

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Author Contributions: Dr Bleasdale had full access to all of the data in the study and takes responsibility for the integrity of the data and of the data analysis. Study concept and design: Bleasdale, Trick, Hayden, and Weinstein. Acquisition of data: Bleasdale, Gonzalez, and Lyles. Analysis and interpretation of data: Bleasdale, Trick, Lyles, Hayden, and Weinstein. Drafting of the manuscript: Bleasdale, Trick, Gonzalez, and Lyles. Critical revision of the manuscript for important intellectual content: Bleasdale, Trick, Lyles, Hayden, and Weinstein. Financial Disclosure: None.

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Additional Contributions: Alla Aroucheva, PhD (Rush University Medical Center), Catherine Nathan, MS, Anjum Owaisi, MD (Cook County Bureau of Health Sciences), and Thomas Rice, PhD (Rush University Medical Center and Cook County Bureau of Health Sciences) provided assistance with data collection and laboratory work. We thank the patients and staff members of the MICU of John H. Stroger Jr (Cook County) Hospital for study participation.

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REFERENCES


