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Does Chlorhexidine Bathing in Adult Intensive Care Units Reduce Blood Culture Contamination? A Pragmatic Cluster-Randomized Trial

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Abstract

OBJECTIVE.—To determine rates of blood culture contamination comparing 3 strategies to prevent intensive care unit (ICU) infections: screening and isolation, targeted decolonization, and universal decolonization.

DESIGN.—Pragmatic cluster-randomized trial.

SETTING.—Forty-three hospitals with 74 ICUs; 42 of 43 were community hospitals.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The contents of this publication does not necessarily reflect the views or policies of the US Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US government. The authors assume full responsibility of the accuracy and completeness of the ideas presented.

PATIENTS.—Patients admitted to adult ICUs from July 1, 2009, to September 30, 2011.

METHODS.—After a 6-month baseline period, hospitals were randomly assigned to 1 of 3 strategies, with all participating adult ICUs in a given hospital assigned to the same strategy. Arm 1 implemented methicillin-resistant *Staphylococcus aureus* (MRSA) nares screening and isolation, arm 2 targeted decolonization (screening, isolation, and decolonization of MRSA carriers), and arm 3 conducted no screening but universal decolonization of all patients with mupirocin and chlorhexidine (CHG) bathing. Blood culture contamination rates in the intervention period were compared to the baseline period across all 3 arms.

RESULTS.—During the 6-month baseline period, 7,926 blood cultures were collected from 3,399 unique patients: 1,099 sets in arm 1, 928 in arm 2, and 1,372 in arm 3. During the 18-month intervention period, 22,761 blood cultures were collected from 9,878 unique patients: 3,055 sets in arm 1, 3,213 in arm 2, and 3,610 in arm 3. Among all individual draws, for arms 1, 2, and 3, the contamination rates were 4.1%, 3.9%, and 3.8% for the baseline period and 3.3%, 3.2%, and 2.4% for the intervention period, respectively. When we evaluated sets of blood cultures rather than individual draws, the contamination rate in arm 1 (screening and isolation) was 9.8% (N = 108 sets) in the baseline period and 7.5% (N = 228) in the intervention period. For arm 2 (targeted decolonization), the baseline rate was 8.4% (N = 78) compared to 7.5% (N = 241) in the intervention period. Arm 3 (universal decolonization) had the greatest decrease in contamination rate, with a decrease from 8.7% (N = 119) contaminated blood cultures during the baseline period to 5.1% (N = 184) during the intervention period. Logistic regression models demonstrated a significant difference across the arms when comparing the reduction in contamination between baseline and intervention periods in both unadjusted (P = .02) and adjusted (P = .02) analyses. Arm 3 resulted in the greatest reduction in blood culture contamination rates, with an unadjusted odds ratio (OR) of 0.56 (95% confidence interval [CI], 0.044–0.71) and an adjusted OR of 0.55 (95% CI, 0.43–0.71).

CONCLUSION.—In this large cluster-randomized trial, we demonstrated that universal decolonization with CHG bathing resulted in a significant reduction in blood culture contamination.

Blood cultures are a critical tool to diagnose bacteremia and guide antimicrobial therapy, especially with the increasing threat of multidrug-resistant organisms (MDROs). However, contamination of blood cultures is still a common problem and may represent up to half of all positive blood cultures.[1,2] The Clinical and Laboratory Standards Institute recommends that each facility maintain a contamination rate less than 3%.[3] The American Society for Microbiology's and College of American Pathologists' benchmark for contaminated blood cultures hospital wide is between 2.5% and 3%.[4,5] In recent studies the overall blood culture contamination rate in intensive care unit (ICU) populations ranged from 4% to 5.5%.[6,7] "Contamination" in these reports is defined as the number of contaminated blood cultures divided by the total number of blood culture draws multiplied by 100. Contamination can lead to unnecessary antimicrobial therapy, unnecessary removal of central lines, unnecessary testing, increased length of stay, and increased cost. Bates et al[8] estimated the cost of contaminated blood cultures at $4,500 per episode. Patients with contaminated blood cultures are just as likely to receive antimicrobial therapy as patients with true bacteremia.[9] It has been reported that up to half of patients with false-positive blood cultures for

coagulase-negative staphylococci were treated with antibiotics, usually vancomycin, with an estimated additional cost of approximately $1,000 per patient.[10] This association between contaminated blood cultures and unnecessary antibiotic use, additional laboratory tests, and increased hospital length of stay and excess costs has been confirmed in subsequent studies, with costs as high as $10,000.[11,12]

Contamination of percutaneous blood cultures is thought to be due to the introduction of organisms from the skin of the patient into the collected sample.[13] Inadequate preparation of the skin is thought to be the most common cause of blood culture contamination.[14] This is supported by surveys of the most common organisms in contaminated blood cultures, which represent organisms that are known to be present on the skin of hospitalized patients. The most common contaminant is coagulase-negative staphylococci, which accounts for approximately 75% of contaminated blood cultures, followed by *Propionibacterium* sp., *Micrococcus* sp., *Corynebacterium* sp., *Bacillus* sp. (not *Bacillus anthracis), Micrococcus* sp., viridans streptococci, and γ-hemolytic streptococci (not *Enterococcus* sp.).[4,9,15] Accordingly, interventions that have been studied to reduce contamination are those that could reduce skin bacterial load or reduce the likelihood of inadvertent introduction of skin contaminants into the sample. These include disinfection methods for skin preparation, culture bottle preparation, needle exchange for bottle inoculation, limiting the use of blood drawn from intravenous lines, and the use of dedicated phlebotomy teams.[4] Recently, several studies have suggested that chlorhexidine (CHG) bathing of patients in the ICU may reduce blood culture contamination rates.[16–18]

In our previous publication,[19] we reported that universal decolonization was more effective than targeted decolonization or screening and isolation in reducing methicillin-resistant *Staphylococcus aureus* (MRSA) clinical cultures and bloodstream infections from any pathogen. In this study, we investigated whether these 3 strategies to prevent ICU infections would have an effect on the rates of blood culture contamination.

METHODS

Study Design

The Randomized Evaluation of Decolonization vs Universal Clearance to Eradicate MRSA (REDUCE MRSA) trial was a 3-arm cluster-randomized trial of hospitals in the Hospital Corporation of America (HCA) system. This study compared 3 strategies to decrease MRSA infections in adult ICUs. Elements of the trial design have been previously described.[17] The strategies were limited to the adult ICU and included:

- Arm 1: Screening and isolation: Patients received bilateral nares screening for MRSA upon ICU admission. Contact precautions were employed for patients with a known history of MRSA (either colonization or infection) or a current culture or screening test positive for MRSA. This arm was considered standard of care at the time and in practice since 2007.[18]
- Arm 2: Targeted decolonization: At ICU admission, patients received MRSA screening and contact precautions similar to arm 1. Patients with known MRSA

colonization received decolonization with twice daily intranasal 2% mupirocin ointment and daily 2% CHG cloth baths for 5 days.

- Arm 3: Universal decolonization: There was no screening for MRSA at ICU admission. Contact precautions similar to arm 1 were employed. All ICU patients received twice daily intranasal mupirocin ointment for 5 days plus daily 2% CHG cloth baths for the entire duration of their ICU stay.

This study consisted of a 6-month baseline period from July 1 to December 31, 2009; a phase-in period from January 1 to April 7, 2010; and an 18-month intervention period from April 8, 2010, to September 30, 2011. This study was approved by the Harvard Pilgrim Health Care institutional review board.

Determination of Blood Culture Contamination

For descriptive purposes, we provide the percent of all blood culture draws either by a percutaneous (direct skin puncture) or from an existing intravascular catheter that contained a skin commensal consistent with contamination. The performance of an individual blood culture commonly involves collecting a volume of blood either via venipuncture or from an intravascular catheter and distributing it into 1 or more bottles (eg, an aerobic and anaerobic bottle). However, in keeping with clinical application, all analyses were performed at the level of blood culture sets unless otherwise specified. Blood culture sets were eligible for the determination of contamination if at least 2 ICU-attributed blood cultures were drawn within 2 calendar days of one another. Thus, a single blood culture draw within a 2-day period was excluded from evaluation. Two or more blood cultures during that time window constituted a single set. Only the first eligible set per patient was evaluated. Blood cultures were deemed attributable to the ICU if the draws occurred more than 1 day into the ICU stay through the day of ICU discharge. This attribution window was selected to allow for the first CHG bath to be given in the ICU. We were unable to determine accurately which blood cultures were drawn by venipuncture or from an existing line.

Among eligible blood culture sets, contamination was defined as having 1 or more of the following pathogens isolated from only 1 blood culture within the set: coagulase-negative *Staphylococcus* sp., *Lactobacillus* sp., *Propionibacterium acnes, Corynebacterium* sp., *Bacillus* sp. (not *B. anthracis), Micrococcus* sp., viridans streptococci, and γ-hemolytic streptococci (not *Enterococcus* sp.). Our analysis focuses on the proportion of eligible blood culture sets that had a contamination event across all 3 study arms.

Statistical Analysis

Census and microbiologic information were obtained from the HCA centralized clinical electronic data warehouse. The HCA system uses a single electronic health record (EHR) platform including the microbiology module for test orders and resulting. The contamination rate was calculated as a percentage of eligible blood culture sets.

We used generalized linear mixed models to account for the cluster-randomized design of the trial. In that context, we used logistic regression to assess the treatment arm, period, and arm-by-period interaction effect. The 2-degree-of-freedom test assessing the interaction

addresses the null hypothesis that the change from baseline to intervention period was the same in each arm. Sensitivity analysis included multi-variable covariate-adjusted models that accounted for age, sex, race, insurance type, coexisting conditions, and surgery during the hospital stay. Analyses were performed with use of Statistical Analysis System (SAS) software, version 9.3 (SAS Institute).

RESULTS

Patient characteristics were similar across all groups and between baseline and intervention periods (Table 1). During the 6-month baseline period, 7,926 blood cultures were collected from 3,399 unique patients: 1,099 sets in arm 1, 928 in arm 2, and 1,372 in arm 3. During the 18-month intervention period, 22,761 blood cultures were collected from 9,878 unique patients: 3,055 sets in arm 1, 3,213 in arm 2, and 3,610 in arm 3. Among all individual draws, for arms 1, 2, and 3, the contamination rates were 4.1%, 3.9%, and 3.8% for the baseline period and 3.3%, 3.2%, and 2.4% for the intervention period, respectively.

When we evaluated sets of blood cultures rather than individual draws, the contamination rate in arm 1 (screening and isolation) was 9.8% (N = 108 sets) in the baseline period and 7.5% (N = 228) in the intervention period. For arm 2 (targeted decolonization), the baseline rate was 8.4% (N = 78) compared to 7.5% (N = 241) in the intervention period. Arm 3 (universal decolonization) had the greatest decrease in contamination rate, with a decrease from 8.7% (N = 119) contaminated blood cultures during the baseline period to 5.1% (N = 184) during the intervention period.

Logistic regression models for contaminated sets (Table 2) demonstrated a significant difference across the arms when comparing the reduction in contamination between baseline and intervention periods in both unadjusted (P = .02) and adjusted (P = .02) analyses. All arms showed a reduction in contamination between the intervention period and the baseline period, but universal decolonization resulted in the greatest reduction in blood culture contamination rates, with an unadjusted odds ratio (OR) of 0.56 (95% confidence interval [CI], 0.044–0.71) and an adjusted OR of 0.55 (95% CI, 0.43–0.71). P values in the pairwise analysis were as follows: P = .19 for the comparison of arm 2 with arm 1, P = .11 for the comparison of arm 3 with arm 1, and P = .005 for the comparison of arm 3 with arm 2. Based on the ORs, universal decolonization avoided an additional 26.8 contaminated blood culture sets per 1,000 admissions compared to arm 2 and an additional 12.2 contaminated blood culture sets per 1,000 admissions compared to arm 1. The most common organism associated with contamination was coagulase-negative *Staphylococcus* sp. (85.0%), followed by *Streptococcus* sp. (6.4%) and *Bacillus* sp. (3.0%; Table 3).

DISCUSSION

Contamination of blood cultures can alter the course of a patient's treatment, resulting in outcomes such as inappropriate antibiotic use, longer hospital stays, or increased cost. Evidence suggests that the rate of blood culture contamination could potentially be influenced by interventions that decrease skin bacterial load, such as CHG bathing.

Bleasdale et al[16] examined the effectiveness of CHG bathing to reduce central line-associated bloodstream infections (CLABSIs) in a 2-ICU crossover study. They reported a significant reduction in primary BSIs and a nonsignificant reduction in the incidence of blood culture contamination from 4.3 to 1.8 per 1,000 patient-days. Popovich et al[17,18] have reported significant declines in blood culture contamination rates in both medical ICUs (6.99 to 4.1 per 1,000 patient-days) and surgical ICUs (5.97 to 2.41 per 1,000 patient-days).

In this large cluster-randomized trial, we demonstrated that universal decolonization with CHG bathing resulted in a significant reduction in blood culture contamination. Of interest the 45% reduction in blood culture contamination with universal decolonization is virtually identical to the 44% reduction of all cause bloodstream infections previously reported.[19]

In this study, we observed a decrease in blood culture contamination in all arms of the study, suggesting a secular trend despite the comprehensive efforts to prevent competing interventions during the trial.[19] While we inquired monthly about competing interventions and participating hospitals were instructed to bring any product or practice changes before the study steering committee, it is possible that national attention to skin or line connector preparation prior to phlebotomy, national efforts to support drawing blood by venipuncture whenever possible, and the concept of dedicated phlebotomy teams may have had a secular impact.

Almost all HCA facilities track blood culture contamination rates as a quality indicator, with appropriate action taken when rates are determined to be greater than 3% after blood culture draws. This included reeducation along retraining healthcare professionals' skills on specimen collection and limiting use of blood draws from intravenous lines. Also, to address national guidance for best practice, HCA launched a campaign as part of a patient safety initiative to reduce CLABSIs, emphasizing maintenance of lines including "scrubbing the hub" and standardizing connectors to meet certain design and safety criteria, making it easier to adequately disinfect the hub. This initiative was equally applied across all 3 arms. This initiative, along with tracking contamination rates, probably explains the secular trend noted in this analysis.

We believe that the benefit attributable to universal decolonization (arm 3) relates to reducing patient bioburden by reducing skin colonization[20] since inadequate skin preparation is thought to be the most common cause of blood culture contamination.[4,13] In addition, our protocol included not only cleaning of the skin with 2% CHG cloths but also wiping of the proximal 6 inches of the line, including the connectors and hubs, with 2% CHG cloths. Coagulase-negative *Staphylococcus* sp. was the most common contaminant in our trial, consistent with other publications.[4,9,15]

The strength of our study was the large size and rigorous design as a pragmatic comparative effectiveness trial implemented primarily through the hospital processes. This design was chosen so that the implementation could be generalized to the broadest set of hospitals with available resources. Our study, however, had several limitations. Since microbiologic data were captured through our early clinical data warehouse, we were not then able to capture clinical signs or symptoms that could be associated with a clinical infection. In

addition we were unable to account for the method of blood draw, including the method of skin cleaning and whether blood cultures were taken peripherally or from an existing line. However, such differences across groups are largely accounted for by comparing the outcome rate in each hospital with that hospital's baseline rate, providing reassurance that the benefit is attributable to decolonization rather than to baseline variation in case-mix or clinical practices across groups.

In conclusion, our study, along with other studies, clearly demonstrated that CHG bathing has a role in decreasing blood culture contamination rates. As this study showed, interventions targeted at different outcomes, such as the reduction of bloodstream infections, can also drive improvements in the rate of blood culture contaminations. Reduction of blood culture contamination can improve the quality of blood culture results and can prevent unnecessary antibiotics, decrease cost, and decrease length of stay.

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TABLE 1.

Patient Characteristics by Strategies to Reduce Blood Culture Contamination in Intensive Care Units

	Baseline, 6 months, *N* = 3,399				Intervention, 18 months, *N* = 9,878			
Variable	**Arm 1**	**Arm 2**	**Arm 3**	***P***	**Arm 1**	**Arm 2**	**Arm 3**	***P***
Admissions with ICU stay and blood draw set	1,099	928	1,372	…	3,055	3,213	3,610	…
Draws per patient, median (IQR)	2 (0)	2 (0)	2 (0)	.6	2 (0)	2 (0)	2 (0)	.5
Length of hospital stay, days, median (IQR)	15 (15)	14 (15.5)	15 (16)	.6	14 (13)	14 (14)	14 (14)	.9
Length of ICU stay, days, median (IQR)	8 (11)	8 (10)	8 (11)	.2	8 (10)	8 (10)	8 (10)	1.0
Age, years, median (IQR)	64 (23)	65 (22)	63 (26)	.5	64 (23)	65 (24)	63 (24)	.5
Female	43.1	44.3	45.6	.6	42.3	45.3	44.5	.4
Race				1.0				1.0
White	73.0	75.1	67.1	…	73.9	74.5	66.9	…
Black	14.9	12.8	10.6	…	14.6	12.9	10.0	…
Hispanic	4.6	8.5	16.9	…	4.7	8.9	18.8	…
Asian	2.7	1.0	1.1	…	2.7	1.1	0.6	…
Other	2.3	1.3	2.5	…	2.5	1.0	2.4	…
Unknown	2.5	1.3	1.9	…	1.6	1.6	1.3	…
Insurance				1.0				1.0
Medicare	56.1	60.3	56.9	…	58.1	60.9	57.1	…
Commercial	23.0	19.4	19.3	…	20.7	18.1	18.9	…
Medicaid	11.0	13.1	13.7	…	10.7	11.0	11.5	…
Self-pay	5.9	4.3	5.2	…	6.3	6.5	6.4	…
Free care	2.1	2.3	2.8	…	1.5	2.0	3.4	…
Other	1.8	0.5	1.5	…	2.6	1.3	2.2	…
Unknown	0.0	0.0	0.5	…	0.1	0.1	0.5	…
Comorbidities								
COPD	29.7	30.4	28.1	.9	31.3	30.9	29.0	.9
Diabetes	29.8	32.8	30.1	.7	30.4	32.1	29.9	.6
Congestive heart failure	30.5	34.4	28.1	.4	30.7	31.8	29.2	.9
Renal failure	22.9	25.4	24.1	.8	25.0	26.8	24.4	.8
Myocardial infarction	83.7	81.3	83.7	.5	83.5	83.1	83.4	1.0

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Variable	Baseline, 6 months, *N* = 3,399				Intervention, 18 months, *N* = 9,878			
	Arm 1	Arm 2	Arm 3	*P*	Arm 1	Arm 2	Arm 3	*P*
Cerebrovascular disease	15.6	17.7	17.6	.7	17.0	14.3	18.0	.3
Peripheral vascular disease	9.3	10.1	10.6	.5	8.6	10.1	11.0	.1
Cancer	10.3	11.1	10.2	.8	9.2	10.4	11.7	.3
Hemiplegia/paraplegia	6.6	7.0	7.0	.9	6.8	6.1	7.1	.9
Liver failure	6.8	9.2	6.0	1.0	4.1	4.7	3.6	.4
Peptic ulcer disease	4.0	4.5	3.4	.7	3.4	3.4	3.3	1.0
Rheumatologic disease	1.7	3.0	3.1	.1	2.2	2.6	3.5	.03
Dementia	1.7	1.7	2.6	.3	2.3	2.3	2.5	.6
AIDS	0.7	0.5	0.9	.8	1.4	0.7	0.8	.03
Surgery during admission	42.9	42.1	48.3	.9	40.0	41.4	47.2	.5

NOTE. All data shown are percentages, unless otherwise indicated. COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IQR, interquartile range.

Table 2.

Results from Logistic Regression Models for Blood Culture Contamination

	Arm 1	Arm 2	Arm 3	Overall trial
	OR (95% CI)	OR (95% CI)	OR (95% CI)	*P*
As randomized, unadjusted	0.74 (0.58–0.94)	0.94 (0.72–1.23)	0.56 (0.44–0.71)	.02
As randomized, adjusted by no. of draws	0.74 (0.58–0.95)	0.93 (0.71–1.23)	0.56 (0.44–0.71)	.02
As randomized, adjusted by no. of draws, age, sex, race, payer, surgery, and comorbidities	0.73 (0.57–0.94)	0.93 (0.7–1.22)	0.55 (0.43–0.71)	.02
As treated, unadjusted	0.74 (0.58–0.94)	0.93 (0.71–1.22)	0.56 (0.44–0.71)	.02
Randomization to all 3 arms, unadjusted	0.75 (0.58–0.96)	0.9 (0.68–1.19)	0.56 (0.44–0.71)	.03
Accounting for randomization strata, unadjusted	0.73 (0.58–0.94)	0.94 (0.72–1.23)	0.56 (0.44–0.71)	.02
Weekday draws (entire set collected on weekday)	0.77 (0.57–1.05)	0.82 (0.6–1.13)	0.56 (0.41–0.76)	.18
Weekend draws (any in set collected on weekend)	0.66 (0.44–0.99)	1.2 (0.72–1.98)	0.56 (0.39–0.83)	.06
Day draws (entire set collected 5 am–4:49 pm)	0.71 (0.5–1.02)	0.97 (0.68–1.39)	0.64 (0.46–0.9)	.24
Night draws (any in set collected 5 pm–4:59 am)	0.79 (0.56–1.11)	0.9 (0.59–1.37)	0.44 (0.31–0.62)	.01

NOTE. *P* values in the pairwise analysis were as follows: $P = .19$ for the comparison of arm 2 with arm 1; $P = .11$ for the comparison of arm 3 with arm 1; and $P = .005$ for the comparison of arm 3 with arm 2.

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TABLE 3.

Blood Culture Contamination Pathogens by Genus Group

	Baseline			Intervention			
	Arm 1	**Arm 2**	**Arm 3**	**Arm 1**	**Arm 2**	**Arm 3**	**Total**
Aerococcus sp.	0	0	0	1 (0.3)	0	0	1 (0.1)
Bacillus sp. (not *anthracis*)	5 (3.1)	4 (3.6)	6 (4.1)	9 (2.7)	8 (2.3)	8 (3.5)	40 (3)
Corynebacterium sp.	2 (1.2)	3 (2.7)	3 (2.1)	8 (2.4)	9 (2.6)	5 (2.2)	30 (2.3)
Diphtheroids	3 (1.9)	0	1 (0.7)	5 (1.5)	2 (0.6)	0	11 (0.8)
Lactobacillus sp.	0	0	0	0	1 (0.3)	1 (0.4)	2 (0.2)
Micrococus sp.	1 (0.6)	0	2 (1.4)	4 (1.2)	3 (0.9)	3 (1.3)	13 (1)
Peptostreptococcus sp.	0	0	1 (0.7)	2 (0.6)	0	2 (0.9)	5 (0.4)
Propionibacterium sp.	0	0	2 (1.4)	3 (0.9)	4 (1.2)	0	9 (0.7)
Saccharomyces sp.	2 (1.2)	0	0	1 (0.3)	0	0	3 (0.2)
Staphylococcus, coagulase-negative species	136 (84)	93 (83)	128 (88.3)	274 (83.3)	293 (85.7)	196 (86)	1,120 (85)
Streptococcus sp.[a]	13 (8)	12 (10.7)	2 (1.4)	22 (6.7)	22 (6.4)	13 (5.7)	84 (6.4)
Total pathogens	162	112	145	329	342	228	1,318

NOTE. All data are no. (%). Multiple pathogens per specimen were allowed.

[a]Viridans group and gamma hemolytic *Streptococcus*, not *Enterococcus sp.*

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