Impact of unit-wide chlorhexidine bathing in intensive care on bloodstream infection and drug-resistant organism acquisition

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ABSTRACT

Background: Chlorhexidine gluconate (CHG) bathing has been reported to decrease bloodstream infections and colonisation of multidrug-resistant organisms (MROs) in intensive care units (ICUs). However, its effectiveness in an Australian setting has not been assessed.

Objective: To test whether the introduction of ICU-wide CHG bathing in place of triclosan would affect rates of the primary outcome of central line-associated bloodstream infections (CLABSI), or the secondary outcomes of ICU-acquired positive blood cultures or other clinical specimens, and MRO colonisation including methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE).

Methods: We conducted a single-centre, sequential, before-and-after observational study. Patient microbiological and clinical data were compared in the 12 months before and after the introduction of CHG bathing in the ICU.

Results: A total of 4262 ICU admissions were studied, 2117 before and 2145 during the CHG-bathing period. There were no significant changes in the rates of CLABSI (from 1.69/1000 central venous catheter-days [95% CI, 0.68–3.48] to 1.33 [95% CI, 0.49–2.90]; $P = 0.68$), or ICU-acquired positive blood cultures (from 5.14/1000 patient-days [95% CI, 3.45–7.39] to 4.45 [95% CI, 3.00–6.36]; $P = 0.58$). However, we observed a lower incidence of MRSA acquisition during the CHG-bathing period (mean difference, –2.13 [95% CI, –3.65 to –0.60] per 1000 patient-days; $P = 0.007$). There was no difference in the rate of isolates involving other pathogens including VRE.

Conclusions: In a tertiary Australian ICU, routine CHG bathing compared with triclosan did not affect the rates of ICU-acquired CLABSI or positive blood cultures. However, it significantly decreased the incidence of MRSA acquisition.

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Hospitalised patients treated in intensive care units (ICUs) are at high risk of health care-associated infections due to invasive treatments such as central venous catheterisation, urinary catheterisation and mechanical ventilation.[1] These infections are associated with increased lengths of stay, costs and mortality, and are particularly concerning in units with a high burden of multidrug-resistant organisms (MROs), including methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE).[2-4] Infection control interventions, including hand hygiene, care bundles to improve line insertion procedures, and active screening and isolation of patients colonised with such organisms, have been used to reduce such health care-associated infections.[5] The use of unit-wide patient bathing with chlorhexidine gluconate (CHG) is an additional strategy that has been studied in ICUs to reduce health care-associated infections.[6-17] Overall, meta-analyses on the effectiveness of this strategy have shown reductions in certain MRO acquisition and in the rate of central-line associated bloodstream infections (CLABSI).[18-20] However, the results have varied among the published studies[6,8-15,17,21] and it has been postulated that this variability may be affected by the baseline prevalence of MRO and infection rates.[19,20,22] The objective of this study was to evaluate the impact of daily CHG bathing in the ICU on the incidence of CLABSIs and ICU-acquired positive blood cultures or ICU-acquired colonisation or positive clinical specimens for key potential pathogens, including MRSA and VRE.

We hypothesised that, in our low risk setting, CHG would not further reduce rates of CLABSI, ICU-acquired positive blood culture and MRO acquisition compared with triclosan bathing.

Methods

The project was approved by Austin Health Human Research Review Committee (LNR/14/Austin/23) and the study was registered on the Australian and New Zealand Clinical Trials Registry (ACTRN12615000101583).

Study design

This was a single-centre, sequential, before-and-after observational study involving patients admitted to an adult tertiary ICU between 1 March 2013 and 31 March 2015. The ICU cares for medical and surgical patients, including cardiac and gastrointestinal surgery, liver transplantation and haematology and oncology patient groups. Unit-wide CHG bathing was introduced into the ICU at the beginning of March 2014, thus dividing patients into a pre-intervention period (1 March 2013 to 28 February 2014) and a post-intervention period (1 April 2014 to 31 March 2015) and allowing for a 1-month lead-in before commencing the post-intervention study period.

During the pre-intervention period, standard practice was for all patients admitted to the ICU to receive daily bed washes with triclosan 1% (Perrigo Australia [former Orion Laboratories], Balcatta, WA, Australia). At the bedside, nurses mixed the contents of a 40 mL triclosan 1% bottle with warm water in a basin and patients were bathed from the neck down. In March 2014, CHG 2% body wipes (Reynard Health Supplies, Artarmon, NSW, Australia) were introduced as the standard wash product for all ICU patients during their admission to the unit and triclosan 1% wash was removed from the ICU.

During the intervention period, CHG wipe-based bathing was completed according to the manufacturer instructions. Before the post-intervention study period, nursing staff received education on the proper technique for bathing with the CHG wipes, and bedside posters were used to reinforce appropriate procedure. Compliance with the use of triclosan 1% and CHG 2% wipes was audited by tracking ICU product usage on a monthly basis. For the purpose of monitoring, either one bottle of triclosan 1% or one pack of CHG 2% wipes were considered to indicate one patient bath.

Throughout the study, nursing staff routinely obtained active surveillance cultures, which consisted of swabs from the nares and/or groins of patients for MRSA and from the rectal area for VRE routinely on admission and then at least weekly during ICU admission. All swabs were processed in the hospital's microbiology laboratory using standard culture-based or molecular-based identification for MRSA and VRE. All patients found or known to be previously colonised with MRSA or VRE were placed on routine contact precautions, with appropriate hand hygiene measures according to the World Health Organization recommendations.[23] All other microbiological samples sent for culture were performed at the treating physician's discretion and according to hospital policy and practice.

All other infection control and cleaning procedures were performed and monitored according to hospital infection control policy throughout the study period. Hand hygiene compliance auditing was conducted routinely by infection control practitioners by observing 350 moments for hand hygiene in ICU per month. Periodic staff hand hygiene education occurred throughout the study period. National protocols for the insertion of central venous catheters (CVCs) were in place and remained consistent throughout the study period.[24]

All patients admitted to the ICU during the study period were included. Patient demographic, clinical and microbiological data were retrospectively extracted from the hospital electronic database for analysis.

Study outcomes and definitions

The primary outcome was the incidence of ICU-acquired CLABSI during the observation period. Cases of CLABSI were collected and assessed routinely based on the Victorian Healthcare Associated Infection Surveillance System (VICNISS) definitions.[25] The VICNISS CLABSI surveillance module is based on methods and definitions used by the Centers for Disease Control and Prevention/ National Healthcare Safety Network.[26] There were no major changes to the CLABSI definition over the study period.

An ICU-acquired positive blood culture specimen was defined as the first positive blood culture for various pathogens including MRSA and VRE obtained more than 48 hours after admission to the ICU. Recurrent episodes in the same patient were excluded. ICU-acquired incident cases of MRSA and VRE colonisation or infection were defined as no previous history of MRSA or VRE, and an active surveillance culture or clinical specimen showing growth of MRSA or VRE was obtained more than 48 hours after ICU admission. An ICU-acquired positive clinical specimen was defined as the first positive clinical culture for a recognised pathogen detected more than 48 hours after admission to the ICU.

Statistical analysis

Data were analysed using STATA software version 11.2 (StataCorp, College Station, TX, USA). We summarised data as medians and interquartile ranges (IQRs) or as numbers and percentages. We used the Mann–Whitney test and χ^2 test or Fisher exact test to compare data between groups. CLABSI rates were reported using the denominator of 1000 CVC-days. Other infection rates were presented as number of infections per 1000 patient-days (95% CI). Incidence rate difference between groups was also calculated. We assessed the CHG effect on ICU-acquired positive cultures using multivariable logistic regression analysis adjusting for the following covariates: age, sex, APACHE (Acute Physiology and Chronic Health Evaluation) III score, mechanical ventilation on admission, admission diagnosis (operative *v* non-operative) and comorbid conditions. We did not apply multivariable analysis to other outcomes due

Table 1. Baseline demographics and clinical characteristics (all ICU admissions)

Characteristic	Available data (*n*)	Control period (*n* = 2117)	CHG period (*n* = 2145)	*P*
Age, years	4262	64 (52–74)	64 (52–75)	0.23
Male sex	4262	1271 (60.0%)	1376 (64.2%)	0.006
APACHE III score	4248	50 (36–66)	49 (36–65)	0.03
ICU admission source	4262			< 0.001
Operating room		1115 (52.7%)	1054 (49.1%)	
Emergency department		363 (17.2%)	411 (19.2%)	
Ward		373 (17.6%)	405 (18.9%)	
Another hospital		211 (10.0%)	182 (8.9%)	
Another ICU		23 (1.1%)	5 (0.2%)	
Unknown		32 (1.5%)	88 (4.1%)	
Main admission diagnosis	4262			< 0.001
Cardiovascular surgery		469 (22.2%)	408 (19.0%)	
Gastrointestinal surgery		337 (15.9%)	267 (12.5%)	
Respiratory		229 (10.8%)	198 (9.2%)	
Sepsis		159 (7.5%)	150 (7.0%)	
Cardiovascular medical		181 (8.6%)	434 (20.2%)	
Comorbidity	4262			
Cardiovascular		70 (3.3%)	45 (2.1%)	0.02
Respiratory		106 (5.0%)	137 (6.4%)	0.052
Chronic renal failure		61 (2.9%)	117 (5.5%)	< 0.001
Insulin-requiring diabetes		55 (2.6%)	51 (2.4%)	0.64
Liver disease		117 (5.5%)	192 (9.0%)	< 0.001
Immune disease		152 (7.2%)	108 (5.0%)	0.003
Immunosuppressed		145 (6.9%)	169 (7.9%)	0.20
Metastases		112 (5.3%)	116 (5.4%)	0.87
Leukaemia/myeloma		24 (1.1%)	33 (1.5%)	0.25
Mechanical ventilation on admission	4262	1038 (49.0%)	939 (43.8%)	0.001
Biochemistry data				
Creatinine, μmol/L	4173	90 (68–140)	92 (70–135)	0.71
WBC, $\times 10^9$/L	2697	12 (9.2–17)	12 (8.8–16)	0.59
Albumin, g/L	4182	28 (24–33)	28 (24–32)	0.33
Length of stay, days				
ICU		1.7 (0.8–3.6)	1.7 (0.8–3.7)	0.66
Hospital		11 (6–21)	10 (6–20)	0.66
Mortality				
ICU		147 (6.9%)	143 (6.7%)	0.72
Hospital		271 (12.8%)	233 (10.9%)	0.05

APACHE = Acute Physiology and Chronic Health Evaluation. CHG = chlorhexidine gluconate. ICU = intensive care unit. WBC = white blood cell. Values are median (interquartile range) or *n* (%).

the insufficient number of events. Statistical significance was set at $P < 0.05$ (two-tailed).

Results

Baseline characteristics of study admission

We studied a total of 4262 ICU admissions with 2117 admitted before and 2145 after the introduction of CHG bathing. The characteristics of study admissions are summarised in Table 1. Admissions during the two periods had different characteristics. In particular, during the CHG bathing period, patients were more likely to be male, had slightly lower illness severity scores, and received mechanical ventilation less frequently. They were also admitted from different sources, belonged to different diagnostic groups and carried different comorbidities.

Process of care

The process of care features are presented in Table 2. They show that admissions during the CHG bathing period had a greater rate but shorter duration of mechanical ventilation (baseline and ICU-initiated).

Although compliance with hand hygiene policies, independently audited, was similar during the two study periods, the consumption of triclosan implied an average of 0.4 washes per ICU admission day before the introduction of CHG bathing and 1.2 after the introduction of CHG bathing.

Table 2. Process of care and surveillance procedures during ICU admissions

Intervention	Control period ($n = 2117$)	CHG period ($n = 2145$)	P
Mechanical ventilation	1058(50.0%)	947(44.2%)	< 0.001
Median (IQR) duration, hours	15(7–45)	18(8–59)	0.002
Hand hygiene compliance rates per audit period (95% CI)			
March	82.1% (76.2–84.5%)	85.6% (81.6–88.9%)	
June	81% (76.6–84.7%)	75.7% (71–79.9%)	
October	79.8% (75.4–83.6%)	80% (75.5–83.8%)	
Bathing product usage, *n* (per patient-day)	2167 (0.4)	8243 (1.2)	

CHG = chlorhexidine gluconate. CI = confidence interval.

ICU = intensive care unit. IQR = interquartile range.

Study outcomes

The study outcomes are presented in Table 3. During the CHG bathing period, there was no significant difference in the primary outcome of ICU-acquired CLABSI (1.69 [95% CI, 0.68–3.48] *v* 1.33 [95% CI, 0.49–2.90] infections per 1000 CVC-days; $P = 0.68$). Moreover, there was no change in the rate of positive blood cultures while in the ICU. However, there was a significant decrease in the number of MRSA isolates obtained by active surveillance cultures and clinically indicated specimens from 3.02 (95% CI, 1.76–4.83) during triclosan to 0.89 (95% CI, 0.33–1.94) per 1000 patient-days during the CHG bathing period ($P = 0.007$). This decrease was similarly distributed in active surveillance cultures and clinical specimens. Finally, there were no significant changes in VRE isolates.

Due to limited numbers, multivariable logistic regression analysis was only possible of the outcome of positive blood cultures (Table 4). CHG bathing did not significantly affect the rate of ICU-acquired positive blood culture specimens. However, the presence of chronic liver failure, mechanical ventilation and non-operative admission increased the risk of positive blood cultures.

Discussion

Key findings

We performed a sequential before-and-after study of a change in patient antimicrobial skin care from 1% triclosan to CHG 2% body wipes in a tertiary ICU. We found that the rate of ICU-acquired CLABSI was low and was not further reduced by CHG compared with triclosan bathing. Moreover, we found that CHG bathing did not decrease the rate of ICU-acquired positive blood cultures. Finally, we found that CHG bathing did not decrease the rate of VRE detection. However, we found the introduction of CHG bathing was associated with a significant decrease in the rate of MRSA isolation from both surveillance and clinical specimens.

Relationship to previous studies

The use of CHG bathing has been assessed in several studies with contrasting results. In the first multicentre cluster randomised controlled trial, universal CHG bathing in ICU was reported to decrease the incidence of health care-acquired bloodstream infections (BSI) from 6.6 to 4.78/1000 patient-days ($P = 0.007$) and CLABSI from 3.3 to 1.55/1000 catheter-days ($P = 0.004$).[9] In the second cluster randomised controlled trial, the same treatment was reported to decrease the incidence of ICU-attributable BSI infection from 6.1 to 3.6/1000 patient-days ($P < 0.001$).[12] In contrast, a more recent study found no significant decrease

Table 3. Summary of colonisation and infection rates

	Control period (*n* = 2117)		CHG period (*n* = 2145)			
	Rate (95% CI)	No. of events	Rate (95% CI)	No. of events	Rate difference (95% CI)	*P*
Patient-days	5637.6		6738.9			
CVC-days	4141		4500			
CLABSI*	1.69 (0.68–3.48)	7	1.33 (0.49–2.90)	6	–0.36 (–1.99 to 1.28)	0.68
Infections per 1000 patient-days						
Positive blood culture specimens (any pathogen)†	5.14 (3.45–7.39)	29	4.45 (3.00–6.36)	30	–0.69 (–3.13 to 1.75)	0.58
MRSA	0	0	0	0		
MSSA	0	0	0	0		
Staphylococcus epidermidis	3.02 (1.76–4.83)	17	2.82 (1.70–4.40)	19	–0.20 (–2.10 to 1.71)	0.84
VRE	0.18 (0.004–0.99)	1	0.30 (0.04–1.07)	2	0.12 (–0.43 to 0.67)	0.73
Gram-negative bacteria	1.60 (0.73–3.03)	9	1.04 (0.42–2.14)	7	–0.56 (–1.83 to 0.71)	0.40
Candida spp.	0.53 (0.11–1.56)	3	0.74 (0.24–1.73)	5	0.21 (–0.69 to 1.11)	0.67
MRSA colonisation (ASC and/or clinical specimen)†	3.02 (1.76–4.83)	17	0.89 (0.33–1.94)	6	–2.13 (–3.65 to –0.60)	0.007
MRSA clinical specimens	1.60 (0.73–3.03)	9	0.59 (0.16–1.52)	4	–1.0 (–2.15 to 0.14)	0.049
MRSA ASC	1.60 (0.73–3.03)	9	0.45 (0.09–1.30)	3	–1.15 (–2.25 to 0.05)	0.02
VRE colonisation (ASC and/or clinical specimen)†	3.37 (2.03–5.26)	19	4.90 (3.37–6.88)	33	1.53 (–0.77 to 3.82)	0.60
vanA	0	0	0.59 (0.16–1.52)	4	0.59 (–0.04 to 1.23)	0.09
vanB	3.37 (2.03–5.26)	19	4.30 (2.88–6.18)	29	0.93 (–1.27 to 3.14)	0.41
VRE clinical specimens	0.53 (0.11–1.56)	3	1.48 (0.71–2.73)	10	0.95 (–0.19 to 2.10)	0.06
VRE ASC	3.19 (1.89–5.05)	18	3.86 (2.52–5.65)	26	0.67 (–1.44 to 2.77)	0.27
MSSA (any clinical specimen)	1.77 (0.85–3.26)	10	1.63 (0.81–2.92)	11	–0.14 (–1.60 to 1.32)	0.85
Gram-positive bacteria (any clinical specimen)	9.22 (6.89–12.10)	52	7.12 (5.25–9.44)	48	–2.10 (–5.28 to 1.08)	0.20
S. epidermidis (any clinical specimen)	5.14 (3.45–7.39)	29	3.86 (2.52–5.65)	26	–1.29 (–3.64 to 1.07)	0.29
Gram-negative bacteria (any clinical specimen)	10.47 (7.97–13.50)	59	8.16 (6.15–10.62)	55	–2.30 (–5.70 to 1.09)	0.19
Clostridium difficile toxin	0.35 (0.04–1.28)	2	0.59 (0.16–1.52)	4	0.24 (–0.54 to 1.02)	0.59
Candida spp. (any specimen)	5.32 (3.59–7.60)	30	7.72 (5.76–10.12)	52	2.40 (–0.48 to 5.27)	0.10

ASC = active surveillance culture. CHG = chlorhexidine gluconate. CI = confidence interval. CLABSI = central line-associated bloodstream infection. CVC = central venous catheter. MRSA = methicillin-resistant *Staphylococcus aureus.* MSSA = methicillin-sensitive *S. aureus.* VRE = vancomycin-resistant enterococci. * Primary outcome. Denominator is 1000 CVC-days. † An event could include > 1 positive microbiological specimens.

in a composite infection end point, which included CLABSI, in a single-centre, cluster randomised controlled trial (2.9 *v* 2.86 infections/1000 patient-days; *P* = 0.95). In this study, the CLABSI rate was very low in both the control and intervention period (0.21 *v* 0.19/1000 patient-days; *P* = 0.91).[13] A recent meta-analysis of 17 trials evaluating the effectiveness of CHG bathing on infection in the ICU showed a 56% reduction in risk of CLABSI with a number needed to treat of 360 to prevent one CLABSI event in ICUs. Thus, the extent of this effect is clearly dependent on the baseline CLABSI rate, with the number needed to treat increasing accordingly.[19]

Table 4. Multivariable logistic regression analysis showing the association with ICU-acquired positive blood culture specimens

Variable	Odds ratio (95% CI)	*P*
Chlorhexidine bathing	1.004 (0.590–1.709)	0.988
Chronic liver failure	2.226 (1.109–4.471)	0.024
Mechanical ventilation on admission	6.918 (3.283–14.577)	0.000
APACHE III score	1.008 (0.999–1.017)	0.082
Operative ICU admission	0.268 (0.136–0.529)	0.000

APACHE = Acute Physiology and Chronic Health Evaluation.
CI = confidence interval. ICU = intensive care unit.

Implications of study findings

Our findings imply that in patients in the ICU the use of CHG bathing is an effective way of decreasing skin colonisation with MRSA compared with triclosan. They, however, also imply that in an environment with a low incidence of ICU-acquired CLABSI or BSI, the clinical gain is not detectable or very limited in magnitude. Moreover, they imply no effect on VRE isolation.

Study strengths and limitations

This was a pragmatic study which aimed to assess the microbiological impact of the introduction of CHG bathing in a tertiary ICU. The evaluation involved more than 10 000 patient-days and more than 8000 CVC-days providing a robust opportunity to see the effect of the intervention on microbial isolates and our primary CLABSI endpoint. It was conducted in an environment with close microbial surveillance, which continued unchanged throughout the study, enabling a detailed assessment of colonisation and infection before and after the intervention. All microbiological and clinical data were independently obtained and electronically recorded and stored. As such, they provided an objective assessment of the relevant outcome measures. Finally, it was able to show an effect on MRSA colonisation which was both plausible and substantial.

Nonetheless, our study carries some limitations. Firstly, it was not a randomised controlled trial. However, as shown in previous studies, individual randomisation is practically impossible for this kind of intervention. Secondly, it is a single-centre study, thus diminishing its external validity. However, the tertiary ICU in question has all the characteristics of a typical tertiary ICU in high income countries, caring for a mixed cohort of surgical and medical patients, and the findings of our study may logically relate to similar ICUs elsewhere. During the study period, non-investigator nursing staff provided bedside patient bathing and while our assessment of CHG body wipe inventory data implied acceptable and improved compliance when compared with triclosan bed bathing, the quality of the bathing provided was not assessed. Higher use of CHG body wipes was likely due to the comparative ease of application, but waning compliance with CHG daily bathing has been detected previously, highlighting the importance of regular monitoring and feedback to ICU staff.[27] This may reduce the overall treatment effect of CHG bathing. The incidence of the outcome measures under assessment was low before the intervention, decreasing our power to detect an effect. However, our findings are of relevance to similar ICUs with a low baseline rate of CLABSI, ICU-acquired BSI and of resistant organisms and a high level of hand hygiene. In such a setting, assuming a 20% relative risk reduction, close to 32 000 patients would have to be randomised to have a 90% power to detect such an effect. Finally, we found a clear effect on MRSA colonisation despite our limited power, thus providing reassurance that this is an effective intervention to decrease colonisation and clinical specimen isolation with such organisms. In this regard, colonisation with *S. aureus* precedes and predicts subsequent BSI.[28] Furthermore, it has been previously shown that targeted reduction nasal colonisation with *S. aureus* reduces nosocomial infection caused by *S. aureus* by about 50%,[29] hence, by inference, prevention of colonisation may be beneficial. Finally, unlike others,[9] we did not demonstrate an effect on VRE isolation. Given that CHG bathing was applied to skin and that VRE is a gastrointestinal organism, such lack of effect appears plausible.

Conclusions

In a sequential before-and-after ICU study, we found a low overall rate of CLABSI and no effect on CLABSI with CHG compared with triclosan bathing. Moreover, we found no effect on ICU-acquired BSI or the isolation of VRE or other pathogens. However, we found a significant decrease in MRSA acquisition. Our findings imply that, in an environment with a low incidence of ICU-acquired CLABSI or BSI, the use of CHG bathing is as effective as triclosan at decreasing such infections, but is more effective at decreasing MRSA isolates.

Competing interests

Karen Urbancic has sat on an advisory board for Merck Sharp and Dohme.

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