American Journal of Infection Control ■■ (2016) ■■-■■

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major Article

Reduction in hospital-associated methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* with daily chlorhexidine gluconate bathing for medical inpatients

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Key Words:
Nosocomial infection
Horizontal
CHG
Chlorhexidine gluconate

Background: Daily bathing with chlorhexidine gluconate (CHG) is increasingly used in intensive care units to prevent hospital-associated infections, but limited evidence exists for noncritical care settings.

Methods: A prospective crossover study was conducted on 4 medical inpatient units in an urban, academic Canadian hospital from May 1, 2014-August 10, 2015. Intervention units used CHG over a 7-month period, including a 1-month wash-in phase, while control units used nonmedicated soap and water bathing. Rates of hospital-associated methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) colonization or infection were the primary end point. Hospital-associated *S. aureus* were investigated for CHG resistance with a *qac*A/B and *smr* polymerase chain reaction (PCR) and agar dilution.

Results: Compliance with daily CHG bathing was 58%. Hospital-associated MRSA and VRE was decreased by 55% (5.1 vs 11.4 cases per 10,000 inpatient days, $P = .04$) and 36% (23.2 vs 36.0 cases per 10,000 inpatient days, $P = .03$), respectively, compared with control cohorts. There was no significant difference in rates of hospital-associated *Clostridium difficile*. Chlorhexidine resistance testing identified 1 isolate with an elevated minimum inhibitory concentration (8 μg/mL), but it was PCR negative.

Conclusions: This prospective pragmatic study to assess daily bathing for CHG on inpatient medical units was effective in reducing hospital-associated MRSA and VRE. A critical component of CHG bathing on medical units is sustained and appropriate application, which can be a challenge to accurately assess and needs to be considered before systematic implementation.

Infections caused by multidrug-resistant bacteria are a growing concern in Canada, with estimates that 1 in 12 adults admitted to a Canadian hospital are colonized or infected with methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), or *Clostridium difficile*.[1] MRSA and VRE infection and colonization are associated with increased morbidity and mortality and prolonged length of stay.[2] They are also associated with significant costs, with an estimated attributable cost of $17,949 for each case of VRE managed at our institution.[3]

Chlorhexidine gluconate (CHG) is an antiseptic agent with broad-spectrum antimicrobial activity, particularly for gram-positive

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Previous presentation: Preliminary results of this study were presented at IDWeek 2015, October 7–11 2015, San Diego, CA.

Funding/support: Supported by Sage Products, LLP, who donated chlorhexidine gluconate cloths for the duration of the study and provided funding to develop the in-house polymerase chain reaction.

Disclaimer: Sage Products, LLP was not involved in the design and analysis of the study.

Conflicts of interest: None to report

0196-6553/
http://dx.doi.org/10.1016/j.ajic.2016.09.019

bacteria, including MRSA and VRE. Theoretically, routine use of this agent could decrease the overall bioburden of multidrug-resistant gram-positive bacteria on a unit, thereby leading to a decline in hospital-associated transmissions.[4,5] Daily use of CHG in the intensive care unit has been shown to be effective in reducing the rate of MRSA and VRE acquisition and bloodstream infections associated with these organisms.[6-9] Although there are limited studies examining the impact of CHG on general medicine units, preliminary data suggest similar effectiveness.[10]

At our health care facility, which is a tertiary care, inner-city Canadian hospital serving a community affected by multiple socioeconomic issues (injection drug use, poverty, and homelessness) and at risk for MRSA infection and colonization, controlling hospital-associated MRSA and VRE is an ongoing issue.[11,12] Adherence with medical treatment and maintenance of good personal hygiene are complex challenges for patients admitted to hospital. In addition, common among inpatient units, nursing staff must concurrently deal with multiple competing clinical demands and a low nurse-to-patient ratio. In some situations, ideal infection control interventions, particularly patient bathing, are subordinated to higher priority concerns, such as imminent patient and staff safety. Suboptimal hospital infrastructure also contributes to ongoing MRSA and VRE transmission because there are limited numbers of single-bed isolation rooms on inpatient medical units. In this environment, mixed cohorting of patients with MRSA, VRE, or both in multibed rooms occurs because patients are prioritized for single-bed rooms based on numerous factors beyond MRSA and VRE status: patient (eg, febrile neutropenia, cystic fibrosis), infection (eg, pulmonary tuberculosis, disseminated varicella-zoster virus, *C. difficile*), or social (eg, violence risk). As a result, rates of MRSA and VRE remain persistently elevated on medical units despite recommended infection control practices to prevent transmission.[2,13] Based on the inherent challenges of the hospital's physical design and the complexity of care required for the population it serves, we implemented CHG bathing on inpatient medical units at our facility to complement existing infection control interventions for decreasing hospital-associated MRSA and VRE transmission.

METHODS

We conducted a prospective crossover study on 4 inpatient medical units (25 beds each) from May 1, 2014-August 10, 2015. For the purposes of the study, the 4 units were categorized into 2 groups such that geographic separation would be created between the groups. The study period was divided into 2 time periods (phase I: May 1-December 2, 2014; phase II: January 6-August 10, 2015) where units alternated between using the intervention or serving as a control. The intervention consisted of daily bathing with no-rinse CHG cloths (2% CHG Antiseptic Body Cleanser; Sage Products, Cary, IL) over a 7-month period, including a 1-month wash-in phase, compared with nonmedicated soap (Freshscent 0.34 oz Shampoo & Body Wash Packet; New World Imports, Nashville, TN) and water basin bathing as a control. Prior to the starting the intervention, infection preventionists (IPs) and infection control physicians provided an initial training session for nursing leaders before each phase and informal education sessions to the frontline staff during nursing safety huddles or 1-on-1 teaching during both phases. Ongoing support and reminders to staff regarding the proper use of CHG was provided on a weekly basis. Training staff on CHG bathing methodology was based on Agency for Healthcare Research and Quality recommendations.[14] Research ethics board approval was obtained.

For routine patient care of bedbound patients receiving the CHG intervention, daily patient bathing was to be performed by a health care worker with CHG cloths. Ambulatory patients were encouraged to apply the cloths themselves, after receiving instruction by frontline staff and a handout (based on the Agency for Healthcare Research and Quality recommendations) outlining the process for use of CHG cloths. If patients wanted to have a shower, they were instructed to shower and then completely dry off prior to applying CHG. Patients with a history of CHG allergy or those that refused CHG cloths were excluded. Nursing bathing time was based on self-monitored timing of bathing practices using soap and water or CHG. The average nurse to patient ratio was 1:4 to 1:5 during the study period. CHG cloths were available for all patients in the intervention cohort, but routine administration was not always achieved. As a result, CHG cloth compliance was monitored weekly based on CHG inventory in relation to the number of inpatient days, with feedback provided to units weekly. Direct observation of daily bathing with CHG was not performed.

Hospital-associated MRSA and VRE clinical and screening isolates were tracked by the infection prevention and control surveillance systems.[15] All new cases of MRSA or VRE colonization or infection were reviewed by the ICPs to determine if they met criteria for hospital-association: identification >72 hours after admission and no previous admission to our facility in the last 4 weeks. *C. difficile* was also followed as a control based on the premise that CHG does not have established sporicidal activity.[16] MRSA, VRE, and *C. difficile* rates (per 10,000 inpatient days) were compared between intervention and control cohorts. All positive blood cultures collected 72 hours after admission were also compared, as well as those positive for *Staphylococcus aureus* (MRSA and methicillin-susceptible *S. aureus* [MSSA]) and commensal skin flora. Commensal skin flora were defined based on the Clinical and Laboratory Standards Institute definitions.[17] Hand hygiene compliance was monitored on a quarterly basis by ICPs according to World Health Organization guidelines and the gold standard method of direct observation.[18] Number of admissions, inpatient days, mean length of stay, occupancy rates, hand hygiene compliance, and MRSA and VRE admission screening compliance were collected to compare intervention versus control units. Universal admission screening (MRSA: anterior nares, perineum, and open wounds, if any; VRE: rectum) is conducted on medicine units. Screening swabs were assessed in the Medical Microbiology laboratory using MRSA Select (Bio-Rad, Redmond, WA) and chromID VRE (bioMérieux, Marcy l'Étoile, France) chromogenic media. Compliance, specifically whether the screen was collected or not within 48 hours of admission, was assessed by cross-section on a monthly basis by an ICP.

All nosocomial isolates of MRSA from the study period which could be recovered, and all blood cultures positive for MSSA identified >3 days after admission, were included for CHG resistance testing. An in-house developed real-time polymerase chain reaction (PCR) targeting efflux pumps (*qac*A/B and *smr*) suspected to be associated with CHG resistance was developed.[19-22] Isolates were boiled for 10 minutes in 1 mM EDTA, 10 mM TRIS-HCL pH 8.0, 0.25% TX-100, and 0.75% TWEEN 20, and the PCR (Lightcycler 2.0; Roche Diagnostics, Pleasanton, CA) was performed directly on the lysate. CHG minimum inhibitory concentration (MIC) was assessed by agar dilution (1, 2, 4, 8, and 16 μg/mL; chlorhexidine digluconate solution 20% in water; Sigma-Aldrich, Oakville, ON) based on Clinical and Laboratory Standards Institute standards.[23] Isolates with an MIC ≤4 μg/mL were considered susceptible based on previously published reports of the epidemiologic cutoff.[24]

Comparisons were described using χ^2 or Fisher exact tests with cells ≤5, with 2-tailed P values and $P < .05$ considered significant. Statistics were conducted using Stata Statistical Software release 14 (StataCorp, College Station, TX).

RESULTS

Comparison of the descriptive attributes for the intervention and control periods is shown in Table 1. There were no significant