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Major Article

Effect of daily chlorhexidine bathing on the acquisition of methicillin-resistant *Staphylococcus aureus* in a medical intensive care unit with methicillin-resistant *S aureus* endemicity

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Background: Universal decolonization is recommended in intensive care units (ICUs) that have unacceptably high rates of methicillin-resistant *Staphylococcus aureus* (MRSA) despite implementation of basic prevention strategies.

Methods: An interrupted time series study was performed to evaluate the effect of daily chlorhexidine bathing on the acquisition of MRSA in a medical ICU with MRSA endemicity. There was a 14-month control period and a 16-month chlorhexidine bathing period. Segmented Poisson regression analysis was performed to assess the impact of daily chlorhexidine bathing on the incidence density of MRSA. Also, chlorhexidine susceptibility testing with polymerase chain reaction for the *qac*A/B gene was performed on MRSA isolates collected during the chlorhexidine bathing period.

Results: There was a significant reduction in trend (–0.056; 95% confidence interval, –0.095 to –0.017; $P = .005$) of incidence density of MRSA despite a significant increase in both level and trend of MRSA prevalence rates during the chlorhexidine bathing period. However, there was no significant reduction in level of incidence density of MRSA during the interventional period. Minimum inhibitory concentration of chlorhexidine and the detection rates of the *qac*A/B gene for a total of 174 MRSA isolates did not increase during the chlorhexidine bathing period.

Conclusions: Daily chlorhexidine bathing resulted in a significantly decreasing trend of MRSA acquisition rates irrespective of increased MRSA prevalence rates in the medical ICU. There was no shift of chlorhexidine-resistant MRSA strains.

Universal decolonization using daily chlorhexidine bathing alone or in combination with mupirocin is recommended in intensive care units (ICUs) that have unacceptably high rates of methicillin-resistant *Staphylococcus aureus* (MRSA) despite implementation of basic prevention strategies.[1-6] A recent multicenter, cluster-randomized, nonblinded crossover trial conducted in 9 intensive care and bone marrow transplant units found a significant 23% reduction in the combined outcome of MRSA and vancomycin-resistant *Enterococcus* acquisition with daily chlorhexidine bathing, with a

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statistically nonsignificant 19% reduction in acquisition of MRSA.[3] There was also a significant 28% decrease in healthcare–acquired primary bloodstream infection (BSI); however, possibly because of low numbers of infections because of the organism, there was no significant decrease in MRSA BSIs.[3] Another recent cluster-randomized clinical trial conducted in 74 adult ICUs found that treating all patients with daily chlorhexidine baths plus 5 days of intranasal mupirocin significantly reduced MRSA-positive clinical cultures attributed to the ICU by 37%.[4] Although there was a significant reduction in overall BSIs, a nonsignificant reduction in MRSA BSIs was observed in the universal decolonization group.[4] We performed active surveillance culture (ASCs) and preemptive contact precaution (CPs) with enhanced environmental cleaning (EC) for the control of multidrug-resistant organisms transmission in the ICU since June 2012. However, there was no significant change in the acquisition rates of MRSA despite a 14-month implementation of these infection control measures in the medical intensive care unit (MICU), with a MRSA prevalence rate of approximately 26%. Therefore, we investigated whether daily bathing with no-rinse 2% chlorhexidine-impregnated washcloths could prevent the acquisition of MRSA in an MICU with MRSA endemicity.

METHODS

Study design

Study setting

Hallym University Sacred Heart Hospital is a Korean university–affiliated, tertiary care hospital with 829 beds, including 16 beds in the MICU. The MICU is divided into 4 rooms with 4 beds about 2m apart per room. Twenty four registered nurses with 1 duty nurse per room (nurse/patient ratio, 1:4), 6 nursing assistants, and 1 environmental management assistant worked in the MICU. Also, 1 intensivist and 2 internal medicine residents stayed at the MICU. Two infectious diseases specialists had the responsibility for infection control and antibiotic control in the ICU. Two infection control nurses assisted infection control in the ICU. There was a 14-month control period between June 2012 and July 2013 and a 16-month chlorhexidine bathing period between August 2013 and November 2014.

ASCs and preemptive CPs with enhanced EC

ASCs and preemptive CPs with enhanced EC performed during the control period continued during the chlorhexidine bathing period. ASCs for patients admitted to the ICU for >48 hours were performed at time of admission if MRSA was not isolated at clinical or surveillance culture during the previous year, once per week, and at ICU discharge or within 2 days of discharge if MRSA was not isolated at clinical or surveillance culture after ICU admission. The collection of specimens for ASCs was through nasal swabs, and chromogenic medium (chromID MRSA; bioMérieux, Marcy l'Etoile, France) was used for detection of MRSA. Species identification and antimicrobial susceptibility testing were performed using the MicroScan Walkaway-96 system (Siemens, West Sacramento, CA) and the MicroScan Dried Gram Positive Combo Panel Type 28 (Siemens). Average time from acquisition of surveillance swab to reporting of positive culture results was 48-72 hours. Negative ASC results were available the next day.

CPs were started preemptively on all ICU patients, pending the results of ASCs requested at ICU admission, and was discontinued if MRSA was not isolated at surveillance or clinical culture. Warning posts for preemptive CPs were displayed at the head side of the bed of patients. If positive culture results of MRSA were reported, warning posts were maintained until ICU discharge. Hand hygiene according to World Health Organization recommendations and the use of gloves, vinyl gowns, and dedicated medical equipment was done for CPs.[7] Personal protective equipment organizers were used to improve compliance with CPs.

Enhanced EC with wipes for surface disinfection (Clinell universal wipes; GAMA Healthcare, London, UK) consisted of twice-daily cleaning of high-touch area by an environmental management assistant and the cleaning of critical medical equipment by duty nurses 3 times a day. A checklist for EC was used to prevent omission of EC.

Daily bathing with no-rinse 2% chlorhexidine gluconate–impregnated washcloths

Before the chlorhexidine bathing period, all ICU patients received routine daily bed baths with nonmedicated, wet towels according to local ICU policy. Nurses and nursing assistants received education on the proper techniques for chlorhexidine bathing and instructions against using certain lotions or products that may inactivate chlorhexidine gluconate 1 week before the introduction of chlorhexidine bathing. Daily bathing with no-rinse 2% chlorhexidine-impregnated washcloths (Clinell universal wipes; GAMA Healthcare) was performed for MICU patients by both nurses and nursing assistants from August 1, 2013. Washcloths were used in sequential order to bathe all body surfaces according to the manufacturer's instructions, with the avoidance of contact with eyes and genitals. Safety data for most chlorhexidine products have not been established in children (age <18 years).[8] If the patient was <18 years of age, daily bathing with nonmedicated, wet towels was performed and excluded from the analyses. If patients were admitted for <48 hours, they were excluded from the analyses, but did receive chlorhexidine bathing. Duty nurses in the MICU monitored patients for skin reactions and reported them to the investigators, as previously described.[3]

Chlorhexidine and mupirocin susceptibility testing

All of the initial MRSA isolates from surveillance or clinical cultures were shipped to the Department of Laboratory Medicine, Kangdong Sacred Heart Hospital, for antiseptic and mupirocin susceptibility testing. Minimum inhibitory concentrations (MICs) of chlorhexidine against MRSA were determined by the broth microdilution method, in concentrations that ranged from 0.125-256 ug/mL (corresponding to chlorhexidine concentrations of 0.0000125%-0.0256%) for chlorhexidine.[9-11] Concentrations of >256 ug/mL could not be performed because of the solidification of the Muller-Hinton broth by the high level of chlorhexidine. Mupirocin MICs were measured for the range of 0.25 to >1,024 ug/mL by the same methods of chlorhexidine. For each experiment, ATCC43300 MRSA (ATCC, Manassas, VA) was used as a quality control strain. Although MRSA isolates were not collected before the chlorhexidine bathing period, whether chlorhexidine resistance developed during the chlorhexidine bathing period was investigated at a 4-month interval. Also, chlorhexidine and mupirocin susceptibilities were compared between MRSA isolates collected from prevalent cases and those from incident cases during the chlorhexidine bathing period.

Detection of antiseptic and mupirocin resistance gene

The presence of the *qac*A/B and *mup*A genes was determined by polymerase chain reaction with primers previously described.[12,13]

*Molecular epidemiologic analysis (*spa *typing)*

Polymerase chain reaction and DNA sequencing for the *spa* gene were performed according to the recommendation of the Ridom SpaServer (http://spaserver.ridom.de/), with *spa*-1113f and *spa*-1514r primers, and *spa* types were assigned using the SpaServer.