Horizontal Infection Control Strategy Decreases Methicillin-Resistant *Staphylococcus aureus* Infection and Eliminates Bacteremia in a Surgical ICU Without Active Surveillance*

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Objective: Methicillin-resistant *Staphylococcus aureus* infection is a significant contributor to morbidity and mortality in hospitalized patients worldwide. Numerous healthcare bodies in Europe and the United States have championed active surveillance per the "search and destroy" model. However, this strategy is associated with significant economic, logistical, and patient costs without any impact on other hospital-acquired pathogens. We evaluated whether horizontal infection control strategies could decrease the prevalence of methicillin-resistant *S. aureus* infection in the ICU, without the need for active surveillance.

Design and Setting: Retrospective, observational study in the surgical ICU of a tertiary care medical center in Boston, MA, from 2005 to 2012.

Patients: A total of 6,697 patients in the surgical ICU.

Interventions: Evidence-based infection prevention strategies were implemented in an iterative fashion, including 1) hand hygiene program with refresher education campaign, 2) chlorhexidine oral hygiene program, 3) chlorhexidine bathing, 4) catheter-associated bloodstream infection program, and 5) daily goals sheets.

Measurements and Main Results: The prevalence of methicillin-resistant *S. aureus* infection fell from 2.66 to 0.69 per 1,000 patient days from 2005 to 2012, an average decrease of 21% per year. The biggest decline in rate of infection was detected in 2008, which may suggest that the catheter-associated bloodstream infection prevention program was particularly effective. Among 4,478 surgical ICU admissions over the last 5 years, not a single case of methicillin-resistant *S. aureus* bacteremia was observed.

Conclusions: Aggressive multifaceted horizontal infection control is an effective strategy for reducing the prevalence of methicillin-resistant *S. aureus* infection and eliminating methicillin-resistant *S. aureus* bacteremia in the ICU without the need for active surveillance and decontamination. (*Crit Care Med* 2014; 42:2151–2157)

Key Words: bacteremia; chlorhexidine; decontamination; hand hygiene; intensive care units; methicillin-resistant *Staphylococcus aureus*

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a common and lethal multidrug-resistant pathogen that is widespread in ICUs, hospitals, and the community. Since methicillin resistance was first discovered in *Staphylococci* in 1961, numerous infection control measures have been proposed to lessen its prevalence, with some institutions going to logistical and financial lengths to control the organism (1, 2). Active surveillance championed under the heading of "search and destroy" has been used for hospitalized patients in Europe and North America (including Veterans Affairs medical centers and nine U.S. states) (3–8). However, the efficacy of this "vertical" or pathogen-specific infection prevention strategy remains uncertain (8). In addition, it has significant drawbacks, including the financial burden as well as nurse and laboratory workload associated with screening, the delayed patient throughput, reduced healthcare provider contact hours, and social quarantine of the patient associated with contact isolation (9–11).

We report the implementation of a series of "horizontal" or universal infection prevention strategies during the past decade and demonstrate their effectiveness in decreasing the prevalence of MRSA infection in the ICU without the need for active surveillance.

MATERIALS AND METHODS

Setting

Tufts Medical Center is a 415-bed level I trauma and tertiary care center in the major metropolitan center of Boston, MA. The surgical ICU (SICU) is a 10-bed unit staffed by an attending intensive care specialist, a second-year resident, three interns, and up to three medical students at any one time. Central venous catheters were exclusively placed by junior residents supervised by qualified midlevel/senior resident or attending staff. During the study period, the nursing staff consisted of registered nurses, budgeted at an average of 18 hours of direct patient care per day.

Study Population

The primary study cohort consisted of all patients admitted to the SICU from 2005 to 2012. These included patients from the general surgery, trauma, vascular, orthopedic, neurosurgery, otolaryngology, urology, obstetrics and gynecology services, and overflow from the medical ICU. Data were collected from an ICU database fully compliant with the Health Insurance Portability and Accountability Act. The Institutional Review Board of Tufts Medical Center approved the use of these de-identified data without the need for informed consent. From 2005 to 2010, we used the Project Impact database, a database developed by the Society of Critical Care Medicine, and later acquired by Cerner (Kansas City, MO), and recorded Acute Physiology and Chronic Health Evaluation (APACHE) II scores, and from 2010 to 2012, we used the ICU Tracker database by Alere Informatics Solutions (Charlottesville, VA), with APACHE IV scores.

Design

Oral chlorhexidine rinses consisted of 0.12% chlorhexidine gluconate six times per day for mechanically ventilated patients, all of whom also had minimum 30-degree head of bed elevation unless clinically contraindicated. The full oral hygiene program comprises KimVent 24-hour oral care packs (Kimberly-Clark, Roswell, GA). These consist of a 4 hourly oral care protocol with 1.5% hydrogen peroxide oral debriding agent, self-cleaning covered Yankauer catheters, suction toothbrushes, and twice daily 0.12% oral chlorhexidine gluconate rinses. The hand hygiene program requires handwash or handrub with 63% isopropyl alcohol before and after every patient or equipment interaction. Hand hygiene events are recorded by an anonymous ICU observer and monthly compliance rates reported publicly by provider group to all staff to encourage adherence to the protocol. The "central line–associated bloodstream infection" (CLABSI) program involves a nurse-led time-out at the beginning of each catheter placement procedure, use of full sterile technique with complete patient draping and 2% chlorhexidine with 70% isopropyl alcohol skin preparation (Chloraprep; Carefusion, San Diego, CA), use of antimicrobial-coated catheters (ARROWg+ard; Teleflex Medical, Research Triangle Park, NC), and chlorhexidine-impregnated central-catheter dressings. Prior to 2005, we used chlorhexidine biopatch dressings (Johnson & Johnson, Piscataway, NJ), whereas from 2005 to 2012, we used 2% chlorhexidine gel dressings (Healthcare Technology, Ashland, MA). These are changed by the nursing staff under sterile conditions every 7 days or if rendered nonocclusive. All catheters are removed as soon as no longer clinically necessary or via ICU policy by 10 days if not antimicrobially coated (e.g., arterial catheters) or 15 days if antimicrobially coated with chlorhexidine silver sulfadiazine (e.g., triple lumen central venous catheters and vascaths). Daily goals sheets remind house staff to assess the need for said catheters on a daily basis on rounds. Chlorhexidine-sponge-bathing is carried out with 2% chlorhexidine impregnated towels 1–3 times per day.

MRSA infection rates were defined as prevalence of hospital-acquired MRSA infections per 1,000 patient days. This was calculated as the number of MRSA-positive clinical culture specimens (e.g., blood, sputum, wound, bronchoalveolar lavage, pleural or peritoneal fluid, tissue), discounting duplicate specimens (e.g., duplicate blood cultures from the same bacteremia), obtained at least 48 hours after admission to the ICU or within 48 hours after transfer to another unit. Blood culture practices changed in 2010 when it became strongly discouraged to draw blood samples through catheters when obtaining culture specimens. The MRSA infection prevalence strictly reflects isolates collected due to clinical suspicion of infection, not for screening.

Statistical Analysis

A local regression model was fitted to the observed MRSA prevalence rates per 1,000 patient days over time. A change point is defined as a point where a structural change is observed in a time series where the mean of the process before the point differs significantly from the mean after. In addition, an autoregressive integrated moving average (ARIMA) model was used to forecast future rates if current trends were to hold. ARIMA methods are a flexible class of statistical model for time series data that can be formulated as a regression of the present outcome on past outcomes with correlated errors. All analyses were conducted using the statistical software package R version 3.0.2 (12).

RESULTS

The patient populations in 2005 and 2012 were not significantly different, with mean average age of 59 years, 37% of admissions on mechanical ventilation, and similar APACHE II scores (13.4 vs 13.99, respectively). Mean APACHE IV score in 2012 was 49.09. In 2012, 52% of admissions were from the operating room, 30% from the emergency department, and 11% from the floors. The standardized mortality ratio (observed mortality/predicted mortality) trended down from 0.66 to 0.56 over the study period.

Figure 1 shows the infection control measures implemented in the SICU from 2005 to 2012, starting with the hand hygiene program. Compliance with the hand hygiene program ranged from 25% to 100%, achieving our goal of 90% compliance in 47% of months and a minimum of 70% compliance in 92% of months. An education campaign implemented in 2010 in response to deteriorating program compliance (commonly referred to as "protocol fatigue") was effective in returning compliance rates over the subsequent years to the target range. In 2005, oral chlorhexidine gluconate rinses were introduced for mechanically ventilated patients, later expanded in 2009 to a full oral hygiene program. This was followed in 2008 by the CLABSI program. Since 2010, daily goal sheets have been effective reminders to house staff on rounds to assess and document the need for central venous catheters and remove them within the 10-day (noncoated) to 15-day (coated) time limits. Finally, 2% chlorhexidine-sponge-bathing of all ICU patients 1–3 times per day was also implemented in 2010.

MRSA infection incidence declined significantly between 2005 and 2012 from 2.66 to 0.69 infections per 1,000 patient days (Fig. 1). Local regression analysis confirmed the significant decline in MRSA infection incidence as an average decrease of 21% per year, with ARIMA modeling showing that if current trends were to hold, the MRSA infection rates in 2013–2017 would fall from 0.42 to 0.19 per 1,000 patient days (Fig. 2). Time series modeling also showed evidence of a change point in 2008, which may suggest that of the interventions, and the CLABSI program was particularly effective.

Bloodstream infections with MRSA trended down from 2005 to 2012, with not a single case of MRSA bacteremia recorded in all 4,478 patients admitted to the SICU in the final 5 years of the study (Fig. 3).

DISCUSSION

Reducing MRSA infection is important to reducing morbidity and mortality in our hospitals and population. The Centers for Disease Control and Prevention reports over 80,000 incident cases of invasive MRSA in the United States per year, a rate of 26 invasive MRSA infections per 100,000 people per year (13). Hospital mortality rates for ICU patients infected with MRSA are reported up to 36.4% (14). Healthcare-associated MRSA strains are implicated in 91% of MRSA infections, emphasizing the importance of hospital-based prevention and control (15). A recent study on the U.S. national burden of invasive MRSA infection revealed that of all healthcare-associated cases of MRSA infection, 77% presented initially in the community, with 79% of these having been hospitalized in the last year (16). Of those not receiving dialysis, the majority had been hospitalized within the last 12 weeks, and 32% were residents of a long-term care facility, suggesting that the latter are also important targets for implementation of rigorous infection control practices. Patients colonized with MRSA in the ICU are at greatest risk for invasive MRSA and can act as reservoirs for infection once transferred out of the ICU to the general hospital population, making it particularly important to control infection in this setting (17). Hence, our study of hospital-based control is valuable as infection or colonization acquired in the hospital affects incident infection in both inpatient and outpatient settings.

Active surveillance by way of a nasal swab at admission and weekly thereafter was in force

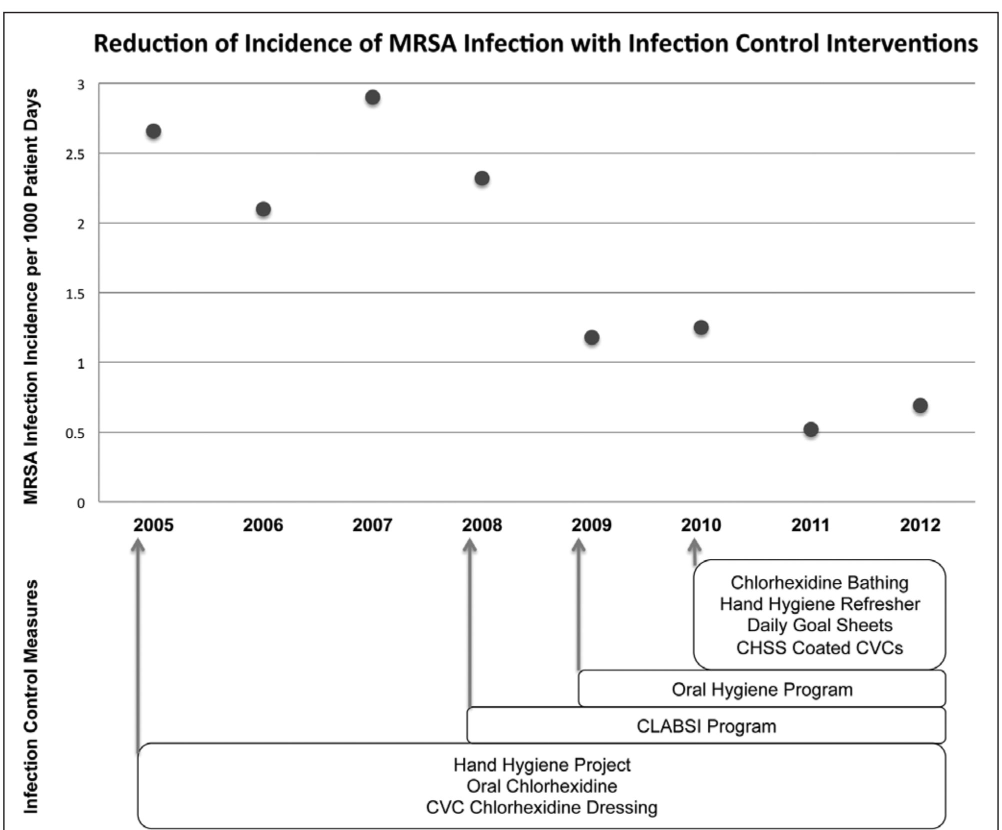

Figure 1. Iterative introduction of horizontal infection control measures over time was followed by a significant reduction in prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections per 1,000 patient days in the surgical ICU. CHSS = chlorhexidine sulfadiazine, CLABSI = central line–associated bloodstream infections, CVC = central venous catheter.

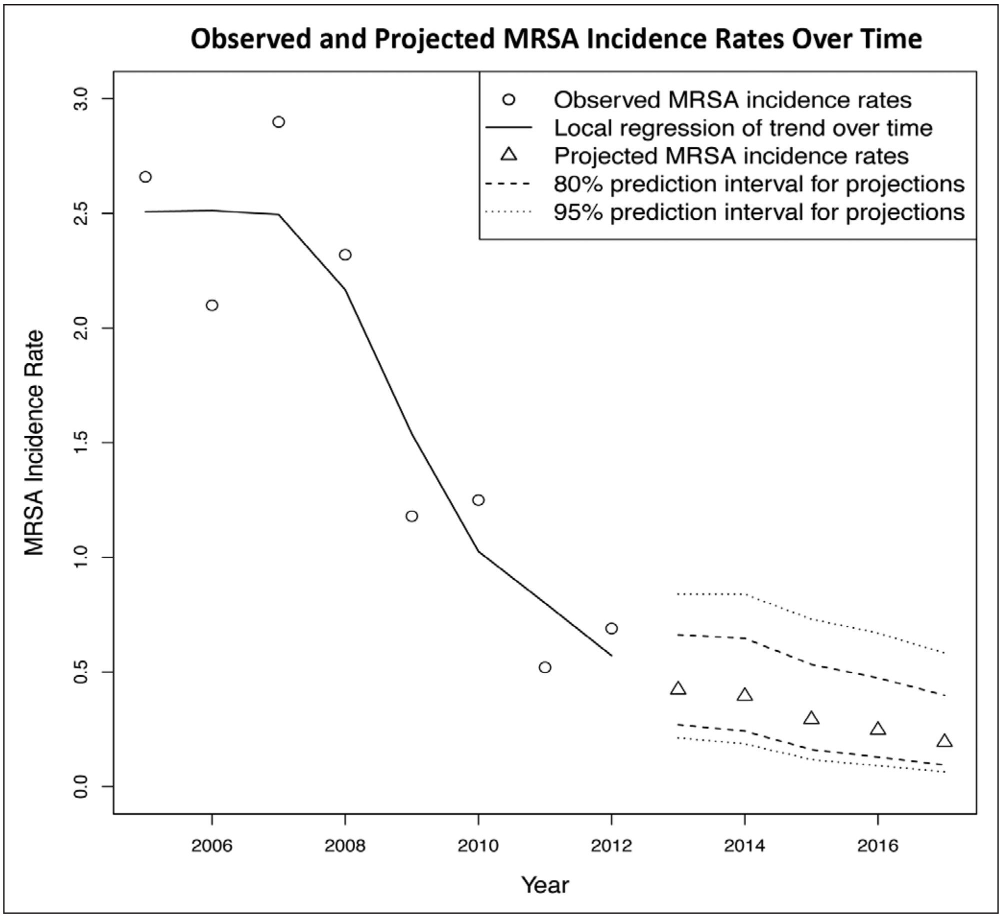

Figure 2. Methicillin-resistant *Staphylococcus aureus* (MRSA) prevalence rates and projected prevalence rates are progressively reduced over time. Projections were informed by an autoregressive integrated moving average model. A change point in the local regression analysis in 2008 may suggest that the central line–associated bloodstream infections program was particularly effective.

from 2000 to 2004 in our SICU. This practice of active surveillance was abandoned when no appreciable decrease in the nosocomial acquisition of MRSA could be demonstrated. Prior to 2005, data on MRSA cultures at Tufts Medical Center were a conglomerate of specimens from active surveillance cultures (implemented 2000–2004), as well as suspected infections. Using said culture data has previously been shown to falsely classify up to 35% of prevalent cases as incident (18). Hence, our study period began in 2005.

We have shown here that the prevalence of MRSA infection can be significantly reduced through a series of evidence-based horizontal infection control measures. MRSA bacteremia has been virtually eliminated from our ICU, an important result since the bloodstream is the second most common site of infection. This has been achieved without the need for vertical or single-pathogen infection control measures such as active surveillance and decontamination.

Vertical Versus Horizontal Infection Control Strategies for MRSA

Patients colonized with MRSA at admission are 17 times more likely to develop a hospital-acquired MRSA bacteremia than those not colonized (19). Vertical infection control strategies try to specifically identify and eliminate cases of colonization. However, although various European governments and the U.S. Veterans Affairs Medical Centers and nine states recommend active surveillance and the "search and destroy" strategy, some studies suggest a lack of efficacy of this approach (8, 20). In a study of 1,232 ICU patients in the United Kingdom undergoing MRSA screening, isolation, and decontamination, there was no significant reduction in MRSA bacteremia (21). A Singaporean study of 653 patients in medical ICU and SICUs also showed no significant reduction in the mean MRSA infection prevalence rate using active surveillance with decontamination strategy (22).

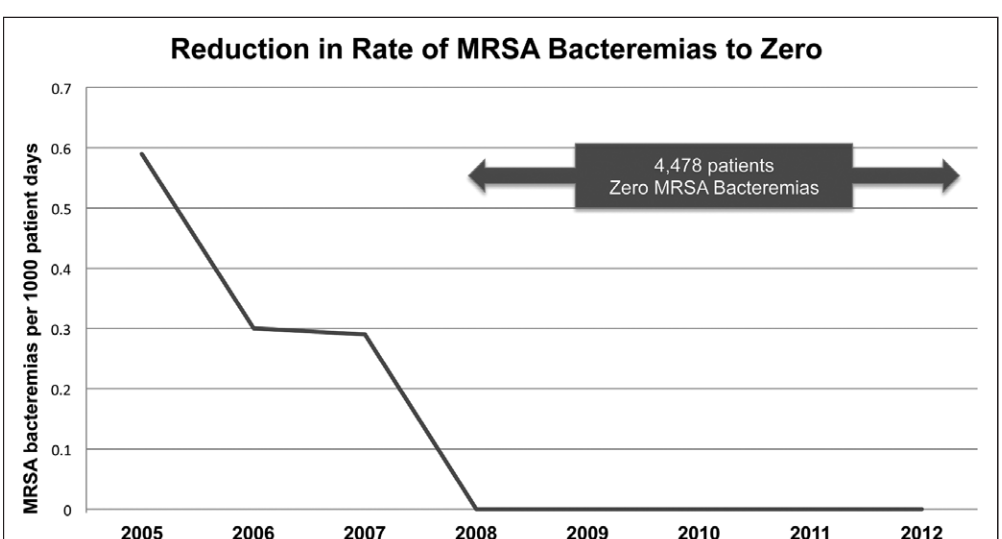

Figure 3. Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia rates fell to zero during the last 5 yr of the study period.

The policy in the Netherlands of screening, treating, and isolating affected patients and healthcare workers and following-up carriers after discharge has had good results; however, it has been accompanied by an added financial cost and increased healthcare worker enforced absences (23, 24).

There are also technical limitations to nasal swab technology in MRSA screening. Low microbial burden, improper swab technique, and the colonization at sites other than those swabbed (usually the nares or groin) could contribute to false-negative results. Depending on the rapidity of processing of MRSA screening swabs, MRSA-positive patients may not be isolated for days prior to their identification by the "search and destroy" method. If all patients are subjected to chlorhexidine decontamination, as with the protocols implemented herein, there is no reliance on swabs, no focus on a single organism as with active surveillance for MRSA, and decontamination generally starts within 12 (chlorhexidine oral care) to 24 (chlorhexidine bathing) hours of ICU admission.

Numerous other issues associated with active surveillance must be considered (5, 6, 19, 23). These include the nurse and laboratory workload associated with screening, the delayed patient throughput during the hospital stay, decreased direct patient care contact hours with providers, social isolation due to fewer visitors, psychological effects (e.g., anger, depression, and anxiety), increased falls, electrolyte disturbances, and decubitus ulcers (9–11, 25). Barrier nursing or isolation may also be logistically difficult secondary to a shortage of single-patient rooms (3, 4).

Horizontal strategies, by contrast to vertical approaches, apply basic infection control interventions to the entire patient population without predetermination of their MRSA status. The burden of harm may very well be greater in a vertical model where all MRSA carriers are isolated than in a horizontal model where only certain infected individuals undergo isolation. In addition, as supported by this study, horizontal or universal strategies are also effective. A recent randomized trial of 74,256 patients in 43 hospitals comparing universal decolonization to targeted decolonization or screening and isolation found that universal decolonization produced a significantly greater reduction in the rate of all bloodstream infections, including MRSA infections, than either of the other two methods (26). In their analysis, the MRSA overall infection incidence was 3.2 per 1,000 patient days for screening and isolation versus 2.1 per 1,000 patient days for universal decontamination (vs 0.69 per 1,000 patient days in the present study). MRSA bacteremia rates were 0.7 per 1,000 patient days for screening and isolation and 0.5 per 1,000 patient days for universal decontamination (vs 0.0 per 1,000 patient days in the present study). The present study demonstrates that implementation of a series of best practice horizontal infection control measures as an integrated strategy is followed by a real reduction in MRSA infections.

Maximizing Efficacy of Horizontal Infection Control Measures

The infection control measures implemented in our ICU included 1) a hand hygiene program with refresher education campaigns to combat protocol fatigue, 2) an oral hygiene program, 3) chlorhexidine bathing, 4) a catheter-acquired bloodstream infection program (including chlorhexidine skin preparation, chlorhexidine-coated central venous catheters, and chlorhexidine-impregnated dressings), and 5) daily goals sheets.

Effective hand hygiene is known to be an important intervention to prevent transmission of bacteria in the hospital environment (27). Hand hygiene programs can be made more effective through employee education, easily available hand gel, regular monitoring of compliance, and feedback to healthcare providers in a public forum of service-specific compliance rates (28). Multiple clinical and modeling studies have concluded that a hand hygiene compliance rate of approximately 70% is the "threshold" for maximally reducing rates of hospital-acquired infection (29). This should be the minimum goal of hand hygiene programs. In the Tufts Medical Center SICU, the goal was 90%, ensuring that the 70% minimum threshold was achieved in greater than 90% of months studied. The culmination of this effort in the final year of this study yielded physician compliance with hand hygiene exceeding 90% for the entire year (28). The importance of fostering a hand hygiene compliant institutional culture, and monitoring this process metric, cannot be underestimated. Some studies' failure to observe a significant reduction in MRSA bacteremia after institution of horizontal infection control measures may, at least in part, be attributed to this (30).

Chlorhexidine was an essential component in several of the infection control measures utilized in the study, including the antimicrobial coating of the central venous catheters, the skin prep used prior to insertion of these catheters, the daily bed baths, and the oral care package. Just as hand hygiene is effective at reducing hands' polymicrobial burden, chlorhexidine is an effective agent against many bacterial pathogens and has been shown to decrease nosocomial infections with MRSA as well as other pathogens, reducing patient length of stay (31, 32). A study of 7,727 patients showed that chlorhexidine bathing was associated with a 23% decrease in multidrug-resistant organism acquisition and 32% decrease in MRSA acquisition (32, 33). One concern is that its daily use on oral, skin, or fomite surfaces (e.g., venous catheters) could select against resistant organisms. Yet a study of 85 MRSA isolates in a Scottish ICU demonstrated no loss of efficacy or increase in resistance in MRSA in the setting of daily bed baths with 4% chlorhexidine gluconate: isolates exhibited stable minimum inhibitory concentrations to chlorhexidine over the 4 years of the study (4). Hypersensitivity reactions to chlorhexidine are uncommon, with 0.47% positive patch testing (34). The most common reaction is a contact dermatitis, making it relatively safe as well as effective for use in the general population (35).

Lastly, several studies have shown daily goal sheets to be effective components of a comprehensive infection control package, reducing infection with multidrug-resistant organisms by improving processes of care (36, 37). These goals sheets are also one of several elements of a culture of safety and quality without which the results of similar infection control programs might be different.

Limitations

We were limited in our ability to prove causality between the observed decrease in MRSA prevalence and our infection control interventions because of the retrospective, observational experimental design used herein. We did not have an appropriate internal control available because all hospital units implemented some (but not all) of the discussed infection control interventions over the course of the study period. Although MRSA rates decreased in all units, the SICU was the most comprehensive with the best results; hence, it was chosen for reporting. Our data are also limited by the fact that the effects of individual interventions are not as clearly distinguished as they would have been if the interventions had been nonoverlapping. Since we did not use MRSA screening at admission, we could not distinguish between hospital acquisition and community colonization, thus potentially overestimating our MRSA acquisition rate. Finally, we are limited by the lack of reliable recording of process metrics on our remaining interventions, aside from hand hygiene compliance data.

Despite these limitations, the decline in MRSA infection is unequivocal and the eradication of MRSA bacteremia without the downsides of the search and destroy strategy is compelling. An ICU MRSA bacteremia rate of zero over a 5-year period is novel and to our knowledge has not been described anywhere else in the literature. Looking to the future, a formal cost analysis would be interesting to evaluate cost efficiency of the described package of infection control measures compared with the active surveillance model.

CONCLUSIONS

MRSA infection is a major burden in hospitals around the world, contributing significantly to the human and logistical costs of healthcare-associated infections. The clinical implication and value of our work is that adherence to protocolized horizontal infection control strategies can successfully and significantly reduce MRSA infection and bacteremia in an ICU while avoiding the additional staff and patient costs of vertical control. The standard of care should be to focus on the "essentials" of horizontal infection control, rather than expending resources on testing, isolation, and decontamination.

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