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Nonimpact of Decolonization as an Adjunctive Measure to Contact Precautions for the Control of Methicillin-Resistant *Staphylococcus aureus* Transmission in Acute Care

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This was an observational study comparing methicillin-resistant *Staphylococcus aureus* (MRSA) transmission with no decolonization of medical patients to required decolonization of all MRSA carriers during two consecutive periods: baseline with no decolonization of medical patients (16 months) and universal MRSA carrier decolonization (13 months). The setting was a one-hospital, 156-bed facility with 9,200 annual admissions. Regression models were used to compare rates of MRSA acquisition. The chi-square test was used to compare event frequencies. We used rates of MRSA clinical disease as an outcome monitor of the program. Analysis was done on 15,666 patients who had admission and discharge tests; 27.9% of inpatient days were occupied by a MRSA-positive patient (colonized patient-days) who received decolonization while hospitalized during the baseline period (this 27.9% represented those who had planned surgery) compared to 76.0% during the intervention period ($P < 0.0001$). The rate of MRSA transmission was 97 events (1.0%) for 9,415 admissions (2.0 transmission events/1,000 patient-days) during baseline and was 87 (1.4%) for 6,251 admissions (2.7 transmission events/1,000 patient-days) during intervention ($P = 0.06$; rate ratio, 0.74; 95% confidence interval [CI], 0.55 to 1.00). The MRSA nosocomial clinical disease rate was 5.9 infections/10,000 patient-days in the baseline period and was 7.2 infections/10,000 patient-days for the intervention period (rate ratio, 0.82; 95% CI, 0.46 to 1.45; $P = 0.49$). Decolonization of MRSA patients does not add benefit when contact precautions are used for patients colonized with MRSA in acute (hospital) care.

Control of infection from methicillin-resistant *Staphylococcus aureus* (MRSA) has been a health care focus for more than 50 years (1). Importantly, by 2005, MRSA-related mortality in the United States was more than that from infections due to salmonella, tuberculosis, influenza, and HIV combined (2, 3). Since that time, efforts to reduce MRSA infection have had impacts in both Europe and the United States (4–6). However, the improvement has not been uniform, with some medical centers not realizing a reduction in disease (7). At least one large state (Illinois) reported an increase in overall rates of MRSA infection during the most recently monitored 5 years, with 11.7 MRSA infections/1,000 hospital discharges in 2009, 11.6 in 2010, 10.7 in 2011, and increasing to 14.2 in 2012 and 13.3 in 2013 (8).

While debate continues over the role of active surveillance testing (AST) for the prevention of MRSA infection (9, 10), it is clear that this approach is widely and successfully used in pragmatic settings (11, 12). One of the reasons that active surveillance testing for MRSA should be expected to be effective is that the greatest risk factor for developing clinical disease is to first become colonized in the nares with MRSA (13). Critically, persons who are either colonized or infected with MRSA are equally likely to have their skin and surrounding environment contaminated with this organism, so it can be readily contracted by others coming close to or touching them (14). Therefore, strategies to limit transmission that consider both colonized and infected persons are most likely to be successful at reducing disease (15).

The recent REDUCE MRSA ("Randomized Evaluation of Decolonization versus Universal Clearance to Eliminate MRSA")

trial suggested that universal decolonization of patients hospitalized in the intensive care unit (ICU) was the optimal approach for preventing MRSA and other multidrug-resistant (MDR) infections (based on assessment of clinical cultures) in that environment (16). One of the concerns raised in the report was the potential development of mupirocin resistance with widespread use (16). We have decolonized inpatients as part of our successful universal admission surveillance program for reducing MRSA infection and have found nearly a 3-fold increase in mupirocin resistance, rising from 3.9% in 2005 to 10.9% in 2012 (I. K. Dusich, et al., presented at the 113th Annual Meeting of the American Society for Microbiology, Denver, CO, 18 to 21 May 2013) (17).

The impact of inpatient decolonization for methicillin-resistant *Staphylococcus aureus* carriers on transmission of MRSA when isolation (contact precautions) is practiced is not well stud-

TABLE 1 Demographics of patients at the study hospital site[a]

	Age (yr)		No. (%) of patients by race/ethnicity[b]						
Sex	Mean	Median (SD)	African American	American Indian or Alaska Native	Asian	Caucasian	Other	Pacific Islander/ Hawaiian Native	Total
Male (44%)	68.7	71.0 (16.7)							
Hispanic/Latino						12 (0)	89 (1)	1 (0)	102 (1.1)
Non-Hispanic			172 (1.9)	8 (0.1)	242 (2.6)	2,837 (30.9)	716 (7.8)		3,975 (43.3)
Total of those who reported race/ethnicity			172 (1.9)	8 (0.1)	242 (2.6)	2,849 (30.9)	805 (8.8)	1 (0)	4,077 (44.4)
Female (56%)	71.1	75.0 (17.4)							
Hispanic/Latino						23 (0.3)	100 (1.1)	3 (0)	126 (1.4)
Non-Hispanic			230 (2.5)	10 (0.1)	355 (3.9)	3,380 (36.8)	994 (10.8)	1 (0)	4,970 (54.2)
Total of those who reported race/ethnicity			230 (2.5)	10 (0.1)	355 (3.9)	3,403 (37.1)	1,094 (11.9)	4 (0)	5,096 (55.6)
Grand total			402 (4.4)	18 (0.2)	597 (6.5)	6,252 (68.2)	1,899 (20.7)	5 (0)	9,173 (100)

[a] Annual admission data for 2011.
[b] No. (%) data are from the 9,173 total.

ied. Our objective was to examine the impact of inpatient decolonization as an adjunct to contact precautions by determining if inpatient nasal decolonization with mupirocin added benefit when contact precautions were used once a person was determined to be colonized with MRSA. Based on the sustained reduction in MRSA clinical disease realized by the U.S. Department of Veterans Affairs health care system using surveillance and contact precautions only, with no decolonization (12, 18), our hypothesis was that, if contact precautions were applied in a timely manner, then decolonization added no benefit. Our study was a quality improvement project designed to test that hypothesis by measuring transmission when decolonization of medical patients was and was not used as an adjunct measure to contact precautions (isolation).

MATERIALS AND METHODS

The study was performed as a before-and-after observational trial at one of four hospitals in the NorthShore University HealthSystem (NorthShore; demographics for patients at this hospital are listed in Table 1). Paired nasal swabs were collected on all inpatients at admission and discharge from April 2010 through August 2012. One swab was used for real-time PCR, following the manufacturer's recommendation (19). The second swab (swab 2) was used for culture, and the result of this was used to determine the rate of MRSA transmission. Swab 2 was plated onto CHROMagar MRSA (CMRSA; BBL, Becton Dickinson, Sparks, MD) and then placed into tryptic soy broth for enrichment that was incubated for 24 h; then the broth was plated to another CMRSA. Mauve colonies were subcultured to a blood agar plate (BBL). *S. aureus* was confirmed using a Staphaurex agglutination test (Remel, Lenexa, KS). Colonies that were latex positive and mauve color were considered MRSA.

Mupirocin ointment (2%) applied to the anterior nares (twice daily for 5 days) plus chlorhexidine (4%; used as a liquid soap) bathing on days 1, 3, and 5 was the decolonization regimen. Before August 2011, inpatient decolonization was not recommended for MRSA colonization, except in presurgical patients (baseline period of 16 months). Starting in August 2011, decolonization was required for all MRSA-positive inpatients (intervention period of 13 months). An MRSA transmission event (TE) was defined as a patient having a negative MRSA culture on admission and a positive MRSA culture at discharge; only those patients with both an admission and discharge sample were included. Patients who had no history of culture-proven MRSA in the prior 2 years and a negative admission test (i.e., those eligible for acquisition) and who had a positive discharge

culture were considered to have newly acquired MRSA. The sample size was powered to detect a 50% reduction in the transmission rate between the baseline and intervention periods. An infection preventionist monitored testing and decolonization therapy throughout the study and immediately intervened whenever compliance with either recommended measure was below 90%.

We also determined the inpatient length of stay (LOS) for those with a positive MRSA admission test and those with a negative test. The inpatient admission MRSA prevalence was determined by dividing the number of patients with a positive culture by the number of tests performed; discharge prevalence was calculated by dividing the number of positive culture patients at discharge plus those with a positive discharge PCR test who were culture positive at admission and decolonized during their stay, divided by the number of tests performed. Finally, a measurement of clinical MRSA disease was performed using the nosocomial infection marker (CareFusion Corporation, San Diego, CA), an electronic surveillance program we previously validated as a reliable tool for monitoring changes in MRSA clinical disease rate (20). Compliance with infection control practices was monitored by the NorthShore infection preventionists, and immediate education given to any hospital staff not following the correct practice.

The chi-square test was used to compare event frequencies between the baseline and intervention groups. A *P* value of <0.05 was considered significant. Analyses were conducted in R version 3.1.1 (21). The two-sample Poisson test was used to determine the difference in MRSA transmission between the two study periods. For our literature review, we used PubMed.gov (Medline) with the search terms MRSA, transmission, and prevention to search the medical literature from 1999 through August 2015. This study was approved by the institutional review board at North-Shore University HealthSystem (protocol EH10-148).

RESULTS

There were 22,548 patients admitted during the entire study period; 13,051 were admitted during the baseline period, and 9,497 were admitted during the intervention period. A total of 19,593 patients were tested at discharge (86.9%). The final analysis was performed on 15,666 patients who had both admission and discharge tests. The rate of admission testing compliance was >90%. However, in January 2012, an electronic prediction rule was implemented that determined who should be screened for MRSA upon admission that captured >90% of potential carriers (22); this resulted in testing of approximately 66% of admissions begin-

TABLE 2 MRSA acquisition data for patients with and without decolonization

Period	% of patients MRSA positive at admission	No. of patients eligible for acquiring MRSA	Patients who acquired MRSA			Eligible patient-days	Acquisition/ 1,000 eligible patient-days	
			No.	%	P^a		No.	P^a
No decolonization of medical patients	6.7	9,415	97	1.0	0.04	47,784	2.0	0.06
Decolonization of medical patients	6.0	6,251	87	1.4		32,298	2.7	
Total	6.5	15,666	184	1.2		80,082	2.3	

^{a} P value for no decolonization versus decolonization.

ning in January 2012. The proportion (percentage) of MRSA-positive patients who had decolonization was 34% during the baseline period (April 2010 through June 2011) and was 82% during the intervention period (July 2011 through August 2012); 100% were decolonized when the length of stay was ≥3 days during the intervention period. The 34% decolonized during baseline represented those who had planned surgery. Since our hospital practice is to decolonize preoperative patients to prevent surgical site infection from *S. aureus* (23), this practice was continued, even though medical patients with MRSA colonization were not decolonized. Decolonization was enforced as a required practice by infection control. Compliance was monitored during the first 6 months of the intervention period by one of the infection preventionists, and of 300 patients who tested positive at admission, 54 were not decolonized; most (50 of 54) of those not decolonized were hospitalized for <1 day, so their positive tests were reported after discharge. The remaining 246 patients were virtually all decolonized (244 of 246; 99.2%) during their hospitalization. Eight patients were colonized with mupirocin-resistant MRSA and 50% of these (four patients) were treated with retapamulin applied in the same manner as mupirocin. The mean and median LOS during baseline were 5.6 and 4.0 days for MRSA-colonized patients and 4.1 and 3.0 days for noncolonized patients, respectively; the mean and median LOS during the intervention period were 5.1 and 4.0 days for MRSA-colonized patients and 4.0 and 3.0 days for noncolonized patients. The combination of this LOS data with the decolonization compliance indicates that, for those colonized, patients received decolonization therapy while hospitalized for 27.9% of inpatient MRSA days (1,226 of 4,396 days) during the baseline period (representing those who had planned surgery) compared to 76.0% of inpatient MRSA-colonized days (1,818 of 2,392 days) during the intervention period ($P < 0.0001$).

The rate of MRSA transmission was 97 (1%) transmission events for 9,415 admissions (2 transmission events/1,000 patient-days) during the baseline period, and it was 87 (1.4%) transmission events for 6,251 of admissions (2.7 transmission events/1,000 patient-days) during the intervention period ($P = 0.06$; rate ratio, 0.74; 95% confidence interval [CI], 0.55 to 1.00). MRSA acquisition data are listed in Table 2. The admission prevalences for MRSA colonization were 6.1% during baseline and 5.5% in the intervention period; the discharge prevalences during baseline and the intervention period were 5.5% (636 positive of 11,555 tests) and 4.7% (371 positive of 7,972 tests), respectively. The MRSA nosocomial clinical disease rate was 5.9 infections/10,000 patient-days in the baseline period and 7.2 infections/10,000 patient-days for the intervention period (rate ratio, 0.82; 95% CI, 0.46 to 1.45; $P = 0.49$). These data, along with the poststudy dis-

ease rate, are depicted in Fig. 1; there was no decolonization of medical patients in the poststudy period, and the clinical disease rate continued to decline. During 15 months of observation after the end of the study (in the poststudy period), the compliance with infection control precautions was 83.0% (1,433 of 1,727 observations) across all NorthShore hospitals. At the facility where this project took place, the compliance was 80.8% (319 of 395 observations).

DISCUSSION

The goal of the NorthShore admission MRSA testing program is to identify patients who are colonized with MRSA and then implement infection control practices, minimizing new MRSA acquisition in order to reduce disease. We assessed the adjunctive benefit of decolonization using mupirocin and chlorhexidine for reducing MRSA transmission in a setting where newly admitted patients undergo rapid screening followed by placement into contact precautions (gown and glove isolation in a private room) for those colonized. Decolonization added no benefit to the placement of patients into contact precautions when evaluated on over 15,600 persons. This indicates that, if one is following the recommended practice of placing MRSA-colonized and/or infected patients into isolation, there is no need to accept the added cost of decolonization or risk the development of antimicrobial resistance by adding antibiotics.

The institution of contact precautions, when adequately followed, raised a sufficient barrier to MRSA dissemination, such
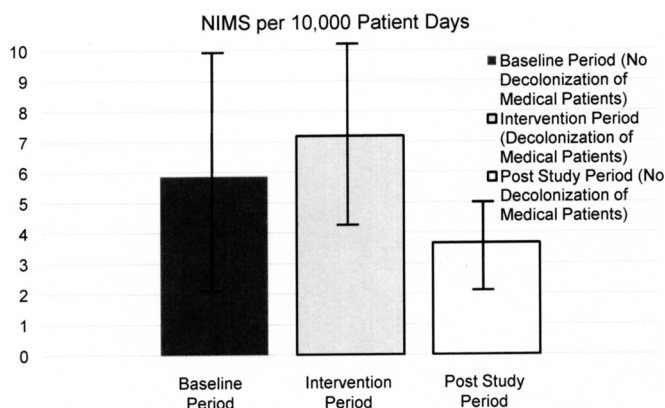

FIG 1 MRSA clinical disease rate over 4.75 years (April 2010 to January 2015) measured using the nosocomial infection marker (NIM) in the baseline period (16 months), the intervention period (13 months), and the poststudy period (28 months). The data are depicted as MRSA clinical disease (NIM) with ± 1 standard error range per 10,000 patient-days.

that the addition of a decolonizing regimen did not positively supplement this effect. The finding is important, since an adverse consequence of using mupirocin for all hospitalized persons would be the risk of development of commonplace mupirocin resistance not only in MRSA but also in methicillin-susceptible *Staphylococcus aureus* strains, which would impair the ability to decolonize preoperative patients carrying this potential pathogen. Decolonizing all *S. aureus* carriers in presurgical patients is an important infection prevention tool, where it has been demonstrated to have a severalfold impact on cost-effectively reducing postoperative infection (23–25). With the deployment of universal MRSA screening in a newly acquired health care facility, we implemented discharge testing in order to determine if mupirocin decolonization was necessary. The data from our evaluation demonstrate that mupirocin does not significantly add to the reduced transmission of MRSA above that achieved from rapid testing and contact precautions. As can be seen from Fig. 1, clinical disease continued to decrease in the postintervention period, when decolonization of medical patients was not done for the hospitalized patients who were not anticipating surgery.

There are three reports that are particularly useful in supporting our conclusion that contact precautions alone are sufficient to impede the spread of MRSA. The first is by Jernigan et al., who found a 15.6-fold reduction in MRSA transmission when contact precautions were applied versus no infection prevention intervention (26). The second study addresses the sustained impact of rapid testing and contact precautions (gown and glove isolation) for the Department of Veterans Affairs hospital system, which monitors the impact of their MRSA control program on 1 million patients per year across the United States (12, 18). Their reported transmission rates of 2 to 2.5 cases per 1,000 patient-days are very similar to our finding, and decolonization is not used in that program. The final report is by Harris et al., who studied a universal contact precaution intervention (without decolonization) in 20 ICUs within 20 hospitals across the United States (27). With an admission colonization pressure somewhat higher than ours (10.5% versus 6.5%), they found a transmission rate of 6 MRSA transmissions per 1,000 patient-days at risk, which is also slightly higher than our rate (Table 2) and the Veterans Affairs rate. Thus, we conclude that decolonization to reduce the spread of MRSA in acute care hospitals is not necessary when contact precautions are rapidly applied. Importantly, for this approach to infection control, the first randomized trial to study adverse events from contact precautions found no association between this practice and additional risk to patients (28).

Expanding the use of universal decolonization for MRSA control in the acute care setting, as suggested in the REDUCE MRSA trial (16), has the potential to limit future use of mupirocin through the development of resistance in staphylococci toward this agent. Presentation of the mupirocin susceptibility trend from this study indicates this is a meaningful risk (M. Hayden et al., presented at ID Week, Philadelphia, PA, 8 to 12 October 2014). During the relatively short 18-month period of study, high-level mupirocin resistance declined for MRSA acquired in the ICU between baseline and intervention periods in both the contact isolation and targeted decolonization arms (from 12% to 9% and from 7% to 5%, respectively) but rose in the universal decolonization arm (from 11% to 16%). The overall difference in differences between arms was significant, at a *P* value of <0.001. This finding should raise concern if mupirocin decolonization were to be used for all

inpatients. Furthermore, as reported by Evans et al. (29), the screening and isolation arm (group 1) had already achieved a 39% decrease in catheter-associated bloodstream infection and a 54% reduction in ventilator-associated pneumonia prior to the start of the REDUCE MRSA trial, demonstrating the impact of screening with targeted application of contact precautions.

Our study has some limitations. Since our investigation was primarily a quality improvement quasiexperimental intervention, there were changes in practice that took place that potentially confounded the measurements of nosocomial MRSA transmission. Specifically, beginning in January, we no longer tested all patients admitted but, rather, applied an automated algorithm to select those patients to be tested (22). This resulted in 34% of admissions not being tested for the final 8 months of the intervention period. Fewer patients tested on admission meant that we could monitor transmission only in those patients actually tested and found to be negative, which could have led to less detected transmission in the intervention (required decolonization of all MRSA-positive patients) arm. In fact, just the opposite was observed: there was a slight, but significant, rise in transmission when measured as patients who acquired MRSA colonization, which demonstrated that the study was not biased by this change in admission testing practice. This observation was interesting and may suggest that decolonizing inpatients could predispose them to new MRSA acquisition. We decolonized based on PCR results that have a 2% to 3% false-positive rate, and our transmission data were based on culture-positive samples; it is possible that some patients were decolonized because of a false-positive PCR and later acquired MRSA during hospitalization, but our study was not designed to measure this. There is growing evidence that the microbiota of the nares is usually colonized by organisms distinct from other regions of the body surface and that reduction of this phylum *Actinobacteria* flora is associated with increased numbers of *S. aureus* and *Staphylococcus epidermidis* (30). Thus, disruption of the usual flora could lead to some risk for MRSA colonization even with targeted decolonization and to a much greater chance for unintended consequences with universal decolonization of the nares. Finally, in order to ensure that any diminished testing did not have a negative clinical impact, we monitored clinical disease development in the baseline, intervention, and poststudy periods. There was no significant change in clinical MRSA disease between the various periods. Importantly, the infection rate continued to slowly decline in the poststudy time frame, as is expected when a new MRSA control program is introduced (12); this decline occurred during a period when no inpatient medical patients were decolonized, further indicating that the change in testing or decolonization practice did not negatively impact the program results or patient care.

A recent report by Schora et al., demonstrated reduced MRSA colonization prevalence (e.g., less transmission) when only targeted decolonization was used for new admissions to long-term care (31). Another report by Das et al. found that targeted decolonization with no isolation prevented MRSA transmission in an inpatient psychiatry unit (32). These studies, taken with our data, suggest the next step in MRSA control for health care organizations. Since our current study indicates that both decolonization and contact precautions (isolation) are not needed for MRSA control, the next logical step would be to perform targeted decolonization without isolation in acute care (throughout the hospital) using an agent that has a low potential for resistance development

to evaluate if this could have the same impact as application of contact precautions in a universal AST setting. If, as suspected, targeted decolonization is as effective as mandated wearing of gowns and gloves for MRSA-colonized or -infected patients, moving to targeted decolonization as a replacement for contact precautions could lower health care cost, improving patient care and health care worker satisfaction. Thus, there is a need for an effective decolonization agent with a low potential for resistance. The active search for such an agent is under way, with some initial success as suggested by experience with a novel synthesized, peptide-mimetic compound causing cell lysis and membrane disruption in *S. aureus* (33); future studies with novel compounds such as this are to be expected.

The quality improvement investigation described in this report demonstrated that mupirocin and chlorhexidine decolonization does not add benefit to an active surveillance testing program where patients found to be positive for MRSA colonization are placed into contact precautions (gown and glove isolation). The addition of decolonization raises the risk of unnecessary antibiotic resistance development, increases cost, and adds one more task for the health care workers in caring for their patients. At the conclusion of this investigation, the hospitals of NorthShore University HealthSystem discontinued inpatient decolonization for all patients who were not anticipated to undergo surgery.

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