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Role of Decolonization in a Comprehensive Strategy To Reduce Methicillin-Resistant *Staphylococcus aureus* Infections in the Neonatal Intensive Care Unit: An Observational Cohort

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Staphylococcus aureus is a common cause of infection in hospitalized neonates. Management of these infections has become complicated by the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) strains.¹ MRSA infections in United States neonatal intensive care units (NICU) increased over 300% between 1995 and 2004.² Strategies to manage MRSA in the NICU include hand hygiene, cohorting and isolation, periodic surveillance cultures, and screening healthcare workers.³

In response to a cluster of MRSA infections in the 42 bed, level four NICU at The Johns Hopkins Hospital in April 2007, the Department of Hospital Epidemiology and Infection Control initiated a comprehensive infection prevention and control strategy. The program included admission surveillance cultures on children transferred from outside hospitals and weekly cultures in all patients, cohorting and isolating MRSA colonized patients, and reinforced hand hygiene, environmental cleaning, and strict contact precautions. In June 2007, decolonization (intranasal mupirocin for all neonates and topical chlorhexidine baths for infants greater than 36 weeks gestational age or greater than 4 weeks chronological age) was recommended for MRSA colonized infants. In July 2007, healthcare workers were screened

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and carriers decolonized. Our objectives were to measure the incidence of MRSA infections over time and to assess the contribution of MRSA decolonization in preventing nosocomial MRSA infections.

We retrospectively identified patients in the NICU who grew MRSA or methicillin-susceptible *Staphylococcus aureus* (MSSA) from any culture obtained between January 1, 2002 and June 30, 2009. Healthcare-associated MRSA and MSSA infections met the criteria established by the National Healthcare Safety Network (NHSN).⁴ Incidence rates for MRSA and MSSA infections were calculated as number of infections per 10,000 patient-days, and rates before and after the intervention were compared using Poisson regression with a linear spline term. Characteristics of patients colonized with MRSA after June 1, 2007 including occurrence of MRSA infection were collected. Comparisons were made using Fisher's exact test and Wilcoxon rank-sum test with a 2-tailed *P* value of <0.05, using Stata version 10.0 (Stata Corp., College Station, TX). The institutional review board approved this study.

From January 2002 to June 2009, 60 patients in the JHH NICU had a healthcare-associated Staphylococcal infection. Forty-three patients (72%) had MSSA infections and 17 (28%) had MRSA infections. There was an increased trend in MRSA infections between 2002 and 2007 (IRR 1.54, 95% confidence interval [CI] 1.04–2.29), but no increased trend in MSSA infections (IRR 1.04, 95% CI 0.84–1.29). After initiation of our comprehensive MRSA control program in 2007, there was a significant reduction in the trend of MRSA infections (*P*=0.04), but not a reduction in the trend of MSSA infections (*P*=0.82).

From June 2007 through June 2009, 29 patients were identified as MRSA carriers. Four patients were identified upon unit discharge, one patient was identified upon developing an MRSA infection; 24 patients were eligible for MRSA decolonization. Sixteen colonized patients (67%) received intranasal mupirocin of whom five received at least one topical chlorhexidine bath. There were no differences in demographic or clinical characteristics between patients who were treated and those who were not treated with intranasal mupirocin [see Table 1]. During 615 days of follow up time for these 24 MRSA colonized patients in the NICU, there were four MRSA infections; one in the mupirocin treated group and three in the not-treated group (IRR 0.08, 95% CI 0.002–1.03).

Between 2002 and 2007, our tertiary care NICU experienced a 54% average annual increase in incidence of hospital-acquired MRSA infections. After introduction of a comprehensive infection control and prevention strategy to identify and cohort MRSA carriers and attempt MRSA decolonization, there was a significant reduction in the trend of MRSA infections.

Active surveillance culturing for MRSA carriers in combination with isolation and decolonization has been used to control MRSA transmission and reduce MRSA infection rates.^{5–7} Screening alone may not be effective in controlling endemic MRSA in the NICU.⁸ Our findings agree with previous studies demonstrating that a comprehensive MRSA control strategy including MRSA decolonization significantly reduced rates of MRSA infections.^{5–7}

A “search and destroy” strategy is mostly reserved for units with high MRSA prevalence or frequent hospital-acquired MRSA infections despite adherence to best practice infection prevention measures.⁹ The role of MRSA decolonization in multifaceted MRSA control strategies is difficult to quantify.¹⁰ Our findings suggest MRSA infection rates may be lowered by MRSA decolonization with intranasal mupirocin with or without chlorhexidine baths; however, our cohort had few MRSA infections and our result did not achieve statistical significance. Whether MRSA infections in hospitals are reduced by screening and isolation (search) or decolonization (destroy) or a combination of both (search and destroy) requires further study. As MRSA becomes endemic in NICUs⁸, as evident by six epidemiologically

distinct strains circulating in our NICU over a two year period [data not shown], we must optimize infection prevention strategies.

Our investigation is limited by its observational design. We did not find differences between mupirocin treated and untreated groups, but we cannot account for factors that might impact a clinician's decision to attempt decolonization. Larger prospective trials are needed to evaluate the impact of MRSA decolonization on infections in hospitalized neonates. As with all retrospective studies, MRSA and MSSA infections may have been misclassified and rates underestimated, but our findings confirm national trends of increasing MRSA infections² and the potential for comprehensive control strategies to reduce MRSA infections. As MRSA becomes endemic in NICUs, further research needs to evaluate best MRSA infection prevention strategies.

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Table 1

Characteristics of Patients Colonized with Methicillin-Resistant *Staphylococcus aureus* (MRSA) Who Were Eligible for Intranasal Mupirocin Therapy

Variable	Patients Treated with Mupirocin (n=16)	Patients Not Treated with Mupirocin (n=8)	P
Demographic			
Gender (female)	7 (44)	5 (63)	0.67
Birth Weight, grams (median, IQR)	875 (700-2555)	1180 (770-2170)	0.84
Gestational Age, weeks (median, IQR)	30 (25-36)	28 (26-34)	0.85
Race			0.42
African American	10 (63)	4 (50)	
Caucasian	4 (25)	4 (50)	
Hispanic	2 (13)	0	
Clinical			
Age at first MRSA culture, days (median, IQR)	46 (23-69)	49 (33-86)	0.62
Days in unit before first MRSA culture (median, IQR)	23 (13-53)	11 (0-51)	0.26
Indwelling central venous catheter at time of first MRSA culture	12 (75)	3 (38)	0.10
Mechanical ventilation at time of first MRSA culture	4 (25)	4 (50)	0.33
Follow-up time after colonization, days (medians, IQR)	25 (20-38)	13.5 (3-26)	0.11
Outcomes			
MRSA infections (number, %)	1 (6)	3 (38)	0.09

n – number; IQR – interquartile range

Values are reported as number (%) unless otherwise specified