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Association of an Active Surveillance and Decolonization Program on Incidence of Clinical Cultures Growing *Staphylococcus aureus* in the Neonatal Intensive Care Unit

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INTRODUCTION

Staphylococcus aureus (*S. aureus*) remains a leading cause of hospital-acquired infections (HAIs) in neonates.¹ Some neonatal intensive care units (NICUs) use active surveillance cultures (ASC) and decolonization to prevent methicillin-resistant *S. aureus* (MRSA) transmission and infections.² However, methicillin-susceptible *S. aureus* (MSSA) infections occur more frequently and have similar mortality in neonates.³

In The Johns Hopkins' NICU, prior to April 2013, neonates were screened for MRSA colonization and carriers were decolonized.⁴ In April 2013, the program expanded to include MSSA screening and decolonization. Previously, we showed that after implementation of MSSA ASC and targeted decolonization, *S. aureus* clinical cultures and infections decreased.⁴ Our objective was to assess whether the reduction was sustained over 3-years.

METHODS

Using the Johns Hopkins Pathology information system, we retrospectively identified neonates admitted to the NICU between April 1, 2011 and June 30, 2016. *S. aureus*-positive clinical cultures were defined as non-surveillance cultures growing *S. aureus*. Cultures from the same patient were considered unique events if collected from the same body site at least 30 days apart or from different body sites at least 14 days apart. NICU-attributable was defined as clinical cultures obtained more than two days after unit admission. Neonates were

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considered to have a bloodstream infection (BSI) if blood cultures grew *S. aureus*. Incidence rates for NICU-attributable *S. aureus* clinical cultures and BSIs and 95% confidence intervals (CI) were calculated for the pre- and post-intervention periods and compared using two-sample Poisson tests. Interrupted time series models were fit to the log-transformed quarterly incidence rates to quantify the immediate impact of the program, and the relative change in incidence rates per quarter during the pre and post-intervention period.⁴ This study was approved by the Institutional Review Board.

RESULTS

During the 24 months before implementation (29,200 patient-days) and 39 months post-implementation (47,135 patient-days), there were 74 and 68 NICU-attributable *S. aureus* clinical cultures, respectively. There were 116 unique patients with 142 *S. aureus* cultures, of which 131 (92%) were MSSA and 11 (8%) were MRSA. Sources for the 142 isolates included 84 (59.2 %) respiratory, 20 (14%) blood, 10 (7.0%) conjunctiva, 11 (7.7%) wound, 7 (4.9%) other, 5 urine (3.5%), 3 abscess (2.1%), and 2 cerebral spinal fluid (1.4%). Post-intervention, 1847 neonates were screened for *S. aureus* colonization as part of the ASC and decolonization program. Of the 333 colonized, 243 were treated with mupirocin.

Overall, a 43% reduction in the incidence rate of *S. aureus* clinical isolates occurred when comparing the post- to the pre-intervention period (IRR: 0.57, 95% CI: 0.40–0.80) (Figure 1a). Prior to the intervention, the incidence rate of *S. aureus* clinical cultures was estimated to increase at a non-significant rate of 14% per quarter (IRR: 1.14, 95% CI: 0.95–1.38). In the quarter following introduction of MSSA to the ASC program, there was an immediate 65% decrease (IRR: 0.35, 95% CI: 0.15–0.82) and thereafter an estimated 2.0% quarterly decrease in the incidence of NICU-attributable *S. aureus* clinical cultures (IRR: 0.98, 95% CI: 0.92–1.05). The rate at which the incidence rates changed over time during the pre- and post-intervention periods did not differ statistically (estimated relative quarterly rate of change: 0.86, p-value: 0.12).

Prior to the intervention, there was no change in the incidence rate of BSIs (IRR: 1.00, 95% CI: 0.78–1.29). After implementation, there were non-statistically significant reductions in the overall incidence rate of *S. aureus* BSIs (IRR: 0.50, 95% CI 0.18–1.34) (Figure 1b), the immediate change in rate of *S. aureus* BSIs (IRR: 0.73, 95% CI: 0.20–2.58) and the quarterly incidence rate of *S. aureus* BSIs (IRR: 0.97, 95% CI: 0.92–1.03).

With an average of 5.5 BSIs per year in the pre-intervention period, 18 BSIs were expected to occur in the post-intervention period, yet we observed 9. In the setting of 70% compliance with the decolonization protocol, 50% fewer infections occurred than expected, suggesting 27 neonates were treated to prevent 1 BSI.

DISCUSSION

Our data suggest an active MSSA screening and decolonization program in the NICU can lead to a sustained reduction (overall 43% decrease) in the incidence of clinical *S. aureus* isolates.

Prior studies have found ASC and decolonization, in conjunction with other infection control measures, can reduce MRSA colonization and infection.^{2,5} Burden of MSSA infections exceed MRSA infections in the NICU,³ yet, few studies have examined the impact of MSSA ASC and decolonization. Recently *Wisgrill et al*⁶ reported promising results of an MSSA surveillance and decolonization program that led to a 50% reduction of MSSA-attributable infections in very low-birth weight infants. Our study reports similar findings, and, we included all neonates admitted to the NICU to reflect the impact on overall burden of *S. aureus* HAIs.

Efficacy, cost-effectiveness and safety influence the decision to perform ASC and decolonization. While there are limited neonatal data, reports from adult populations suggest active surveillance, targeted decolonization, and at times universal decolonization are cost effective when compared to other prevention methods.⁷ Possible unintended consequences of decolonization include replacing *S. aureus* with more virulent pathogens. However, in a multi-center NICU study examining MRSA decolonization, patients treated with mupirocin did not show increased risk of novel Gram negative and fungal infections.⁸ Emerging resistance to mupirocin must also be considered with widespread use, but recent *S. aureus* ASC and decolonization programs have not found an increase in resistance to mupirocin.^{4-6,9}

Incorporating MSSA screening into a NICU's infection control protocol may be an important step to reduce *S. aureus* infections in this vulnerable neonatal population.

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Figure:

(A) Quarterly incidence rate of *Staphylococcus aureus* (*S. aureus*) clinical cultures before (April 1, 2011-March 30, 2013) and after (April 1, 2013-June 30, 2016) implementation of a methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) active surveillance and decolonization protocol. Dashed horizontal lines show the average incidence rate of *S. aureus* during the pre- and post-periods and the dashed vertical line represents start of intervention (Quarter 9). MRSA and MSSA are depicted in black and gray, respectively. (B) Quarterly incidence of *S. aureus* bloodstream infections (BSIs) before and after implementation of a methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) active surveillance and decolonization protocol.