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Concise Communication

Recurrent colonization with methicillin-susceptible *Staphylococcus aureus* after successful decolonization in a neonatal intensive care unit

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Abstract

Recurrent methicillin-susceptible *Staphylococcus aureus* colonization following successful decolonization in a neonatal intensive care unit (NICU) has been observed. Of 17 recolonization events, 53% were due to concordant strains; 19 different *spa* types were identified. Results of this study support sources of re-acquisition both intrinsic and extrinsic to the NICU.

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Introduction

Staphylococcus aureus (SA) is the most common pathogen of healthcare-associated infections in neonatal intensive care units (NICUs), causing both outbreaks and sporadic infection. Methicillin-susceptible SA (MSSA) strains cause more infections than methicillin-resistant SA (MRSA) strains.[1] Colonization is a recognized risk factor for infection.[2] Active surveillance cultures and decolonization of colonized infants have been shown to decrease overall rates of SA infections in the NICU.[3–6] However, after successful decolonization, infants hospitalized in a NICU may become recolonized.[5–8] The source for recurrent colonization may be intrinsic to the NICU (eg, equipment, personnel, environment) or extrinsic (eg, parents, visitors).[3,9] There are few studies examining the genetic relatedness of colonizing MSSA strains isolated prior to and after decolonization.[8] The objective of this study was to determine whether MSSA strains recolonizing infants after successful decolonization are similar or different from the original colonizing strain.

Methods

Setting and design

This was a retrospective study of prospectively collected clinical and epidemiologic data conducted from May 1, 2017 through September 17, 2019 in a 57-bed Level IV NICU housing 2–10 infants/room where active weekly surveillance culture and decolonization for both MSSA and MRSA was implemented in April 2017.[7] Combined cultures were obtained from the anterior nares, umbilicus, and inguinal region. MRSA-colonized infants were placed on contact isolation. Colonized infants underwent decolonization with mupirocin ointment applied to both nares, umbilicus, and any abraded skin twice daily for 10 doses. Weekly active surveillance was continued for the duration of hospitalization.

Decolonization was defined as having two or more consecutive negative weekly surveillance cultures following initiation of mupirocin treatment. Infants receiving anti-MSSA systemic antibiotics were excluded. Recolonization was defined as growth of MSSA form surveillance culture following successful decolonization. Eligible infants were those colonized with MSSA who were successfully decolonized, became recolonized, and for whom both isolates were available for analysis. The Northwell Health Institutional Review Board approved this study with a waiver of informed consent.

Electronic medical record

Demographic and clinical factors were abstracted from the electronic medical record, including age, dates of colonization and recolonization, and level of respiratory support.

Microbiologic and molecular laboratory methods

BD BBL CultureSwab was used for surveillance sampling. Surveillance swabs were cultured on CHROMID MRSA/CHROMID SA bi-plate (bioMerieux, USA). Molecular methods were performed on paired isolates from recolonized infants and MSSA isolates from a sample of NICU staff who were screened due to their epidemiological link to infants colonized with MRSA. Staphylococcal protein A (*spa*) typing was performed by PCR and Sanger sequencing. *Spa*-types were assigned using the Ridom Staph

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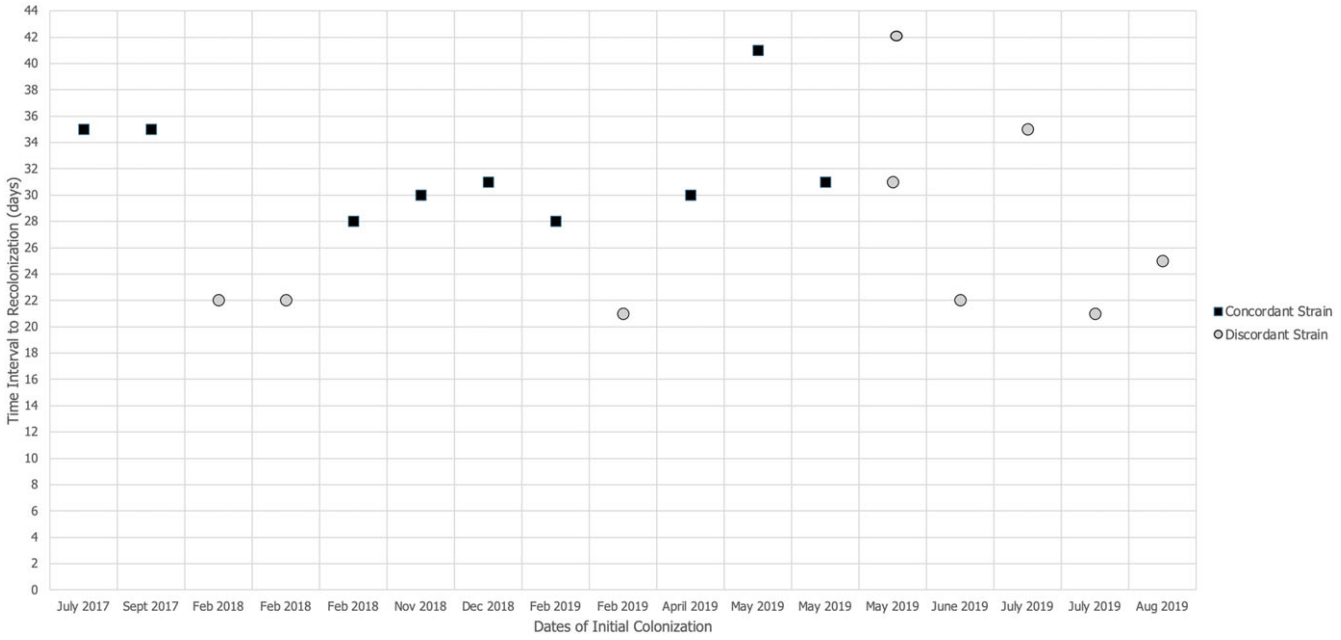

Figure 1. Dates of initial colonization and time interval to recolonization with methicillin-susceptible *Staphylococcus* aureus among infants recolonized with concordant (■) or discordant (◯) strains.

Database (Ridom, Germany). Isolate pairs with the same *spa* type were subjected to whole genome sequencing (WGS; Illumina MiSeq) and phylogenetic analyses as previously described.[10,11] Pairs of isolates with <25 single nucleotide polymorphism (SNP) differences were considered closely related (concordant). Pairs of isolates with different *spa* types or with the same *spa* type but ≥25 SNP differences were discordant.[12]

Results

During the 22.5 months study period, 261 infants were newly colonized with MSSA with a mode of 2/week (range, 0–11/week) and median weekly positive rate of 10.2% (range, 0–25.53%). Isolates from 67 infants were available for typing and 38 different *spa* types isolates were identified. The most frequently detected *spa* types were t148 (6 patients), t3841 (6 patients), and t002 (5 patients). In 26 patients, recolonization occurred with a total of 36 occurrences. Study eligibility was met for 17 occurrences in 16 infants. The median gestational age and chronological age at the time of recolonization was 28 weeks and 10 weeks, respectively. In 12 (71%) cases the infant was receiving respiratory support at the time of recolonization, 11 with nasal prongs and 1 with endotracheal tube.

Among the 34 before and after isolates, 19 different *spa* types were identified of which *Spa* type t002 was the most frequent. In 9 (53%) of the 17 recolonization events the recolonizing isolate was concordant with the initial isolate (Figure 1). Of these, at the time of recolonization, 7 (78%) were on respiratory support, 6 with nasal prongs, and 1 with endotracheal tube. In 8 (47%) the initial and subsequent isolates were discordant including one pair of isolates with the same *spa* type but with 31 SNP differences. Of these, at the time of recolonization, 5 (63%) required respiratory support, all with nasal prongs.

During the study period, SA colonization among selected NICU staff yielded 17 MSSA isolates that were analyzed; 15 unique *spa* types were identified, one of which was the same *spa* type as an infant recolonized with a concordant strain.

Discussion

Recurrent SA colonization following successful decolonization of infants in a NICU has been demonstrated,[6–9] but few studies focused on MSSA.[8] The finding that approximately one-half of episodes of recurrent colonization is due to genetically closely related strains is lower than that the 66% observed by Akinboyo et al. among infants recolonized with MSSA.[8] In their study successful decolonization was defined as a single negative surveillance culture (compared to at least 2 negative cultures in this study); therefore some of their patients may have had persistent colonization rather than decolonization and recolonization. In patients experiencing recolonization with closely related strains, the source may be parents/visitors[9] rather than NICU personnel in view of the heterogeneity of MSSA strains cultured from our NICU patients and staff. However, colonization of parents/visitors was not assessed; therefore this study does not provide direct evidence that tests this hypothesis.

The rate of recolonization following successful decolonization in MSSA colonized infants in our NICU was 14% which is lower than recolonization rates of 34% and 72% reported in other studies.[7,9] This may be due to differences in criteria used to define recolonization. Our definition was stringent in that 2 negative interim cultures were required for and infants receiving anti-MSSA systemic antibiotics when obtaining cultures were excluded to avoid classifying infants as decolonized when colonization may have been suppressed, but not eradicated, by anti-MSSA antibiotics. Weekly screening compliance of approximately 98% suggest that lower rates of recolonization was not due to missed opportunities for screening.[5]

Risk factors for SA recolonization have not been extensively evaluated, although use of respiratory equipment has been reported to be a risk factor.[8] Data regarding presence of invasive devices in recolonized infants was not abstracted and the analysis of risk factors for recolonization was beyond the scope of our study; however, among infants with recolonization, we did not find a

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significantly increased risk of recolonization with a concordant strain in those with respiratory equipment. Hand hygiene adherence was greater than 90%, making this an unlikely contributing factor to recolonization.

Limitations to this study include its retrospective nature, single center design, and small sample size, potentially limiting generalizability of the study. Surveillance culturing techniques may vary between providers wherein poor collection may decrease the sensitivity of a positive surveillance swab. Similarly, with weekly surveillance, a surveillance culture may be obtained while an infant is completing their decolonization treatment, which may also decrease its sensitivity. However, our requirement for 2 negative surveillance cultures should reduce this potential limitation. Furthermore, infants may be colonized in sites (eg, anal) that were not sampled in the surveillance cultures. Another limitation is that, due to availability of isolates, only 47% of episodes of recolonization were included, which reduced the sample size and may limit generalizability of the findings.

SA, particularly MSSA, is a common organism colonizing infants in a NICU. The results of this study support sources of reacquisition both intrinsic to the NICU and extrinsic from parents/visitors. Given the occurrence of recolonization, continued surveillance following successful decolonization is important to maximally reduce SA infections. It is likely a multitargeted approach is necessary to reduce colonization and recolonization including infection prevention measures that incorporate staff hand hygiene, environmental maintenance and possibly decolonization of frequent visitors.

Data availability statement. This data was previously presented at IDWeek 2021.

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Competing interests. None.

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