JPPT | Single Center Retrospective Study

Implementation of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Nasal Polymerase Chain Reaction (PCR) Screening in Pediatric Patients for De-escalation of Antibiotics

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OBJECTIVE Recent literature supports the use of methicillin-resistant *Staphylococcus aureus* (MRSA) nasal polymerase chain reaction (PCR) screening to guide de-escalation of anti-MRSA antibiotics. The objective of this study was to expand on the limited pediatric data, encouraging the use of MRSA nasal PCRs as a tool to guide de-escalation of anti-MRSA antibiotics.

METHODS This single center, pre- and post-interventional, retrospective cohort study compared antibiotic regimens in pediatric patients treated empirically with anti-MRSA antibiotics, with and without MRSA nasal PCRs. Use of MRSA nasal PCRs in the pediatric hospital was encouraged following an antimicrobial stewardship provider-led continuing education presentation. The primary outcome was duration of therapy of anti-MRSA antibiotics in days. Secondary outcomes included positive predictive values (PPVs) and negative predictive values (NPVs) for all infections, pneumonia, and skin and soft tissue infections.

RESULTS A total of 319 patients were included in the study, 252 in the pre-intervention group and 67 in the post-intervention group. The duration of anti-MRSA antibiotic therapy in the pre-intervention group was 6.6 days compared with the post-intervention group at 2.0 days (p value = 0.027). Using data from 38 patients with concordant culture results for the infectious diagnosis, overall NPV was calculated as 92.1%. Skin and soft tissue infections and pneumonia were found to have NPVs of 90.1% (22 patients) and 100% (5 patients), respectively.

CONCLUSION Implementation of MRSA nasal PCRs in pediatric patients significantly reduced the duration of anti-MRSA antibiotic therapy, promoting their utility for antimicrobial stewardship.

ABBREVIATIONS IDSA, Infectious Diseases Society of America; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; NPV, negative predictive value; PCR, polymerase chain reaction; PPV, positive predictive value; SSTIs, skin and soft tissue infections; VAP, ventilator-associated pneumonia

KEYWORDS anti-MRSA; diagnostic; MRSA nasal PCRs; pediatric; retrospective

J Pediatr Pharmacol Ther 2025;30(3):347–351

DOI: 10.5863/JPPT-24-00062

Introduction

The current adult Infectious Disease Society of America (IDSA) and the American Thoracic Society guidelines for community-, hospital-, and ventilator-acquired pneumonia mention use of nasal screening for de-escalation of anti–methicillin-resistant *Staphylococcus aureus* (anti-MRSA) antibiotics.[1,2] These guidelines state that depending on relative patient risks and prevalence of MRSA, a negative MRSA nasal polymerase chain reaction (PCR) result suggests pneumonia is likely not due to MRSA and anti-MRSA antibiotics can be discontinued. It is anticipated that additional data, including other disease states, will be forthcoming about the utility of the MRSA nasal PCRs.

MRSA nasal PCRs have a 96.5% negative predictive value (NPV) for treatment of community-acquired pneumonia, hospital-acquired pneumonia, and ventilator-associated pneumonia.[3] In Mergenhagen et al,[4] de-escalation of anti-MRSA antibiotics in adults was achieved by using MRSA nasal PCRs in several different types of infections including bloodstream, intra-abdominal, respiratory, wound, and urinary. In this study the NPVs were 96.1% for bloodstream and respiratory infections, 98.6% for intra-abdominal, 93.1% for wound, and 99.2% for urinary infections. Because most studies looking at MRSA nasal PCRs took place in adult patients, the question of whether or not these

data are generalizable to the pediatric population remains. In 1 single center retrospective analysis of 95 pediatric patients, MRSA nasal PCRs showed an NPV of 95.5% in multiple types of infections.[5] The objective of this study was to expand on the limited pediatric literature, encouraging the use of MRSA nasal PCRs in pediatric patients as a tool to guide de-escalation of anti-MRSA antibiotics.

Materials and Methods

Study Design. This single center, pre- and post-interventional, retrospective cohort study evaluated pediatric patients who were initiated on anti-MRSA antibiotics for any infection at Prisma Health Children's Hospital – Upstate between March 1, 2022, and August 31, 2022 (pre intervention) and March 1, 2023, to August 31, 2023 (post intervention). As part of Prisma Health- Upstate's pediatric antimicrobial stewardship team, our lead pediatric infectious diseases physician provided a continuing education presentation to pediatric inpatient faculty. The presentation promoted the use of MRSA nasal PCRs, was presented on February 6, 2023, and was used as the intervention of the study. She discussed the benefits and place of therapy for MRSA nasal PCRs, based on existing adult and pediatric primary literature.

Patients in the pre-intervention group were found by using medication administration reports for the included anti-MRSA agents. Patients in the pre-intervention group were not excluded if they received an MRSA nasal PCR. In the post-intervention group, patients were found by using the MRSA nasal PCR usage report for the selected dates, then filtered to patients younger than 18 years. They were included if they were younger than 18 years, admitted for inpatient treatment, and received at least 1 dose of, or were treated with 1 of the following anti-MRSA agents: clindamycin, daptomycin, linezolid, or vancomycin. Excluded patients included those in the neonatal intensive care unit owing to existing hospital protocols screening for MRSA surveillance. Patients receiving the anti-MRSA agents ceftaroline, sulfamethoxazole/trimethoprim, and doxycycline were excluded because these medications, with the exception of ceftaroline, were generally used for disease processes other than MRSA infections, such as *Pneumocystis jirovecii* prophylaxis or tick-borne infections. With ceftaroline being a restricted antimicrobial, it was excluded because it was unlikely for patients to undergo de-escalation. Patients were identified by using administration reports for included anti-MRSA agents, along with a MRSA nasal PCR collection report. No restriction was placed on timing of MRSA nasal PCR collection.

Outcomes. The primary outcome of this study was to compare the median number of days patients received anti-MRSA agents before and after implementation of MRSA nasal PCRs. Secondary outcomes included duration of intravenous (IV) antibiotic therapy, hospital length of stay, number of patients who required surgical interventions for infections, types of infections, comparison of empiric anti-MRSA antibiotics, comparison of oral antibiotic prescribed (if applicable), number of patients with cultures, evaluation of culture results, positive predictive values (PPVs) and NPVs of MRSA nasal PCRs, and specificity and sensitivity of MRSA nasal PCRs.

Statistical Analysis. Continuous variables were assessed with the Wilcoxon rank sum test. Categorical data were assessed with the Fisher exact test. Results are reported as median values (IQR, 25–75). All statistical analyses were analyzed by using SAS statistical software. p values <0.05 were considered statistically significant.

Results

Study Population. A total of 454 patients were screened. There were 252 included patients in the pre-intervention group and 67 in the post-intervention group. Excluded patients included 32 patients discharged from the emergency department, 6 patients admitted to the neonatal intensive care unit, and 54 patients who did not receive an anti-MRSA antibiotic.

Patient demographics are summarized in Table 1. Similarities between the pre-intervention group and the post-intervention groups were observed in terms of sex, age, and hospital length of stay. Differences in the empiric anti-MRSA agent were seen between the 2 groups, with the pre-intervention group using clindamycin more (122 patients [48.41%] vs 13 patients [19.4%]) than the post-intervention group. The post-intervention group did use more vancomycin (123 patients [48.81%] vs 51 patients [76.12%]). More pneumonia infections were found in the post-intervention group (20 patients [7.94%] vs 17 patients [25.37%]). Other infections included bone and joint infections and were seen at a higher rate in the post-intervention group (85 [33.73%] vs 43 [64.18%] patients). Head, eyes, ears, nose, and throat infections were seen at a higher rate in the pre-intervention group (57 patients [22.62%]) vs zero seen in post-intervention group.

Primary Outcome. The primary outcome was total duration of MRSA coverage. The total duration was shorter in the post-intervention group than the pre-intervention group (6.6 days [IQR, 1.5–10.3] vs 2.0 days [IQR, 1.0–8.5]; p = 0.027).

Secondary Outcomes. An NPV for all infections was calculated to be 92.10% and included 38 patients in total. Breaking this down further, 22 of the patients had a skin and soft tissue infection (SSTI) with correlating cultures giving an NPV of 90.1%. An NPV for pneumonia was also calculated at 100.0% and included 5 patients in total. A PPV of 50% was calculated for all infections and included 6 patients (Table 2).

Table 1. Patient Baseline Characteristics

	Pre Intervention (n = 252)	Post Intervention (n = 67)	p value
Male sex, n (%)	131 (52.61)	38 (56.72)	0.550
Hem/Onc, n (%)	39 (15.48)	9 (13.43)	—
Age, n (%)			0.178
<12 mo	22 (8.73)	12 (17.91)	
1–5 yr	99 (39.29)	22 (32.84)	
6–12 yr	68 (29.98)	18 (26.87)	
>12 yr	63 (25.00)	15 (22.39)	
Length of hospital stay, median (IQR), days	3 (2–6)	4 (2–8)	0.081
Type of infections, n (%)			
PNA	20 (7.94)	17 (25.37)	<0.001
SSTI	108 (42.86)	35 (52.24)	0.170
Bacteremia	31 (12.30)	1 (1.49)	0.004
Sepsis	10 (3.97)	2 (2.99)	0.707
CNS infections	18 (7.14)	0 (0.00)	0.024
HEENT	57 (22.62)	0 (0.00)	<0.001
Other	85 (33.73)	43 (64.18)	<0.001
Empiric IV MRSA covering agent, n (%)			
Clindamycin	122 (48.41)	13 (19.40)	<0.001
Daptomycin	4 (1.59)	0 (0.00)	
Linezolid	3 (1.19)	3 (4.48)	
Vancomycin	123 (48.81)	51 (76.12)	

CNS, central nervous system; HEENT, head, eyes, ears, nose, and throat; Hem/Onc, hematology/oncology; IV, intravenous; MRSA, methicillin-resistant Staphylococcus aureus*; PNA, pneumonia; SSTI, skin and soft tissue infection.*

Table 2. Secondary Outcomes

	Pre Intervention (n = 252)	Post Intervention (n = 67)	p value
Length of IV anti-MRSA coverage, median (IQR), days	1.29 (0.66–2.00)	1.00 (0.75–2.00)	0.993
Total duration antibiotic coverage, median (IQR), days	10.00 (6.66–14.00)	10.54 (7.08–17.00)	0.148
Cultures,* n (%)	220 (87.30)	63 (94.03)	0.122
Culture results, MRSA, n (%)	31 (14.09)	5 (7.94)	0.003
Surgical intervention,† n (%)	100 (42.19)	30 (37.97)	0.5092
Narrowed therapy without MRSA results, n (%)	35 (13.94)	—	
Narrowed therapy following MRSA PCRs,‡ n (%)	1 (7.69)	32 (47.76)	0.007

IV, intravenous; MRSA, methicillin-resistant Staphylococcus aureus*; PCRs, polymerase chain reactions*

* Any of the following: blood, wound or abscess, respiratory, urine, cerebral spinal fluid.
† Any surgical intervention aimed at gaining primary source control including but not limited to tooth extractions, video-assisted thoracoscopic surgery, incision and drainage of wound or abscess.
‡ Patient received MRSA nasal PCR, and anti-MRSA therapy was discontinued.

Discussion

The most recent IDSA hospital-acquired pneumonia/ventilator-acquired pneumonia guidelines recommend the use of MRSA nasal PCRs for de-escalation of antibiotic therapy and increased antimicrobial stewardship.[2] The amount of data regarding the utility of this diagnostic test for other indications, including sepsis, SSTI, to name a few, is increasing. The data in previous

trials support the use of the MRSA nasal PCRs, owing to its high NPV of >90%, for most infections.[4,6] This study found a similar NPV for all infections and expanded these data to pinpoint the NPV for pneumonia and SSTIs in pediatric patients. Both pneumonia and SSTIs maintained an NPV of >90% individually.

With the information published, our pediatric providers began using the MRSA nasal PCRs in their daily practice, without an official change to hospital protocols. Our retrospective study found that using MRSA nasal PCR screening decreased the number of days patients received anti-MRSA therapy. The increased antimicrobial de-escalation has the potential to decrease the risk for adverse events associated with anti-MRSA agents and may increase cost savings, based on associated drug monitoring costs, although these endpoints were not evaluated.

The implementation of MRSA nasal PCR testing decreased the number of anti-MRSA antibiotic days, correlating to an increased provider willingness to de-escalate antibiotics when compared with the period before its use. Despite this, providers opted to de-escalate therapy in only about 50% of cases in the post-intervention group. Although specific reasons for providers' reluctance to de-escalate therapy were not captured, this presents an opportunity for future pharmacy-provider education and antimicrobial stewardship involvement. The findings from this study still may lead to a change in protocol, as the adult hospital associated with our campus has a pharmacy-driven protocol for ordering the MRSA nasal PCRs following a vancomycin consult to pharmacy for dosing. In the current adult protocol, the only infections included are those with significant data supporting MRSA nasal PCRs and consist of sepsis, pneumonia, and SSTIs. The results of this study provide rationale for the expansion of this protocol to pediatric patients.

Our study has limitations. First, the small pre- and post-intervention sample size. Owing to the timeline of our intervention, the data collection period was compressed, resulting in the small sample size. Second, the intervention was a one-time, virtual presentation. This led to decreased attendance and limited personal connection and questions. The material was available in slide format for those unable to attend the live presentation, but this still led to limited discussion and is not as effective as other interventional strategies. There were no policy changes implemented owing to the presentation, so the use of the MRSA nasal PCRs relied on changes to individual provider practice. Third, the inclusion of the hematology/oncology population in this study may have skewed the de-escalation results because providers may be less likely to de-escalate therapy in significantly immunocompromised patients. Additionally, trimethoprim-sulfamethoxazole was excluded from the list of anti-MRSA agents owing to its routine use in the oncology population for *Pneumocystis jirovecii* pneumonia prophylaxis. Fourth, determining whether the reason for de-escalation was due to the MRSA nasal PCR or determining the reason for not de-escalating therapy was not able to be collected owing to the retrospective nature of this study and the limitations associated with electronic medical record review in this setting. This information would be beneficial to determine how to educate providers moving forward. Fifth, there was a nationwide IV clindamycin shortage during the post-intervention period, which led to usage discrepancies between the 2 groups. There was also a significant difference in the types of infections treated between the pre- and post-intervention groups, potentially resulting in different de-escalation practices. Lastly, the lack of diagnostic cultures collected resulted in fewer patients being available for inclusion in the NPV calculations.

Conclusions

Use of the MRSA nasal PCRs decreased the number of anti-MRSA agent days in the pediatric population at our center. The calculated NPVs and PPVs of MRSA nasal PCRs for all infections was comparable to those seen in current adult and pediatric literature. MRSA nasal PCRs are a valuable tool for antimicrobial stewardship by providing guidance to support discontinuation of unnecessary antibiotics and preventing resistance. In conclusion, this study demonstrates the utility of MRSA nasal PCRs to guide antibiotic de-escalation in the pediatric population.

Article Information

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Disclosure. The authors declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. The authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors attest to meeting the four criteria recommended by the ICMJE for authorship of this manuscript.

Ethical Approval and Informed Consent. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant international guidelines on human experimentation and have been approved by the appropriate committees at our institution. However, given the nature of this study, informed consent was not required by our institution.

Acknowledgments. The authors acknowledge Alex Ewing and the statistician staff for their assistance with the statistical analysis. These research data collected, including the results, discussion, and conclusion, were presented at the Southeast Regional Conference (SERC) in Athens, GA, on April 25, 2024.

Submitted. June 20, 2024

Accepted. September 14, 2024

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