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ORIGINAL RESEARCH & CONTRIBUTIONS

Nasal Methicillin-Resistant *Staphylococcus aureus* Polymerase Chain Reaction: A Potential Use in Guiding Antibiotic Therapy for Pneumonia

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Perm J 2015 Winter;19(1):34-36
http://dx.doi.org/10.7812/TPP/14-101

ABSTRACT

Context: The role at admission of nasal polymerase chain reaction (PCR) for patients with methicillin-resistant *Staphylococcus aureus* (MRSA) in guiding antibiotic therapy for lower respiratory tract infection is unknown.

Objective: To determine whether nasal MRSA PCR at admission can predict the absence of MRSA in lower respiratory tract secretions.

Design: We performed a retrospective study of adult patients admitted to a large urban hospital. Patients had a nasal MRSA PCR test and a lower respiratory tract culture obtained within 48 hours of admission and the culture yielded *S aureus.*

Main outcome measures: Sensitivity, specificity, and positive and negative predictive values.

Results: Our results showed high sensitivity (93.3%) and negative predictive value (95.2%) of nasal PCR for MRSA in the lower respiratory tract.

Conclusion: With its high sensitivity and negative predictive value, a nasal MRSA PCR test performed within 48 hours of hospital admission could help guide the discontinuation of MRSA-directed empiric antibiotic therapy in patients who are unlikely to be infected with this organism. A prospective study is needed to confirm these findings.

INTRODUCTION

According to published guidelines, hospitalized patients at risk of methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia should receive empiric therapy for MRSA pending culture results.[1] The principal limitations of this approach are that 40% to 70% of patients fail to produce adequate respiratory tract samples, and the processing of sputum specimens takes 72 to 96 hours.[2,3] Therefore, patients empirically initiated on an anti-MRSA antibiotic regimen will certainly receive it for several days and probably remain on it for a full course of therapy. Overuse of antibiotics is associated with increased costs, drug-drug interactions, toxicity, and the development of antibiotic resistance.[4,5] Early identification of patients at very low risk of MRSA infection may spare them empiric antibiotic therapy directed against MRSA.

Nasal screening for MRSA with highly sensitive polymerase chain reaction (PCR) has a turnaround time of about one hour.[6] This test is largely used for epidemiologic purposes; its usefulness as a tool for clinical decision making remains unclear. Nasal PCR results may help guide initial empiric antibiotic therapy for respiratory tract infections because the nasopharynx is generally regarded as the source of pathogens in bacterial pneumonia.

This study addresses a remarkably simple and focused question, namely, whether the absence of nasal colonization with MRSA (using nasal MRSA PCR) can predict the absence of MRSA in lower respiratory tract secretions. We hypothesized that a negative nasal MRSA PCR correlates with the absence of MRSA in lower respiratory tract cultures, when both are collected within 48 hours of admission. If true, these results might guide empiric antimicrobial treatment of lower respiratory tract infection.

METHODS

We conducted a retrospective study of adult patients admitted to an urban teaching hospital (Baylor University Medical Center in Dallas, TX, with 1065 beds including 125 intensive care unit [ICU] beds) from September 2010 through October 2012. Inclusion criteria were 1) age 18 years or older; 2) MRSA nasal swab for PCR obtained within 48 hours of admission; and 3) a lower respiratory tract sample (sputum, tracheal aspirate, bronchoalveolar lavage, or bronchial wash or brush) obtained within 48 hours of hospital admission that yielded *S aureus.* We excluded patients transferred from another acute care facility. During the time of this study, ICU protocol required nurses to obtain a nasal MRSA PCR screen within 24 hours of ICU admission. Non-ICU patients underwent nasal PCR screening for MRSA at physician request. Lower respiratory tract cultures were obtained at the discretion of the physician; hospital protocol did not mandate surveillance cultures. Baylor Research Institute's institutional review

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Table 1. Demographic and clinical characteristics

Characteristic	No. (N = 72)
Age, years (mean)	55
Sex	
Male	42
Female	30
Race and ethnicity	
Non-Hispanic white	32
Non-Hispanic black	29
Hispanic	8
Asian	3
Comorbid conditions	
Diabetes	29
Neurologic disease	24
Obstructive pulmonary disease	18
Cancer	11
Tracheostomy	8
Cystic fibrosis	5
Human immunodeficiency virus	5

board approved the study. The institutional review board granted a waiver of individual informed consent.

Electronic medical records and laboratory data were reviewed. For each patient, we recorded age, sex, race, comorbid medical conditions, ICU admission, and inhospital mortality. The hospital microbiology laboratory (med fusion, Lewisville, TX) provided a list of patients with MRSA nasal PCR results and a second list of patients with lower respiratory tract cultures positive for *S aureus* (sputum, tracheal aspirate, bronchoalveolar lavage, or bronchial wash or brush). Nasal swab PCR for MRSA was processed using BD GeneOhm (Becton, Dickinson and Co, San Diego, CA) until May 2011, and then Roche LightCycler MRSA Advanced Test (Roche Diagnostics, Indianapolis, IN) until the end of the study.[6] Respiratory tract samples were cultured on blood, colistin nalidixic acid, chocolate, and MacConkey agar.

Sensitivity, specificity, and positive and negative predictive values were obtained for nasal MRSA PCR as the diagnostic test and lower respiratory tract culture as the gold standard for detecting MRSA in the lower respiratory tract. We calculated 95% confidence intervals on the basis of logit transformation.

RESULTS

Seventy-two patients met inclusion criteria. Demographic and clinical characteristics are shown in Table 1. Lower respiratory tract samples included sputum (60%), tracheal aspirate (32%), and bronchoalveolar (8%) specimens. Forty-nine (68.1%) patients were admitted to the ICU, and 23 (31.9%) were admitted to the medical ward. Twenty-two (30.6%) patients died during the hospitalization.

Conditional probabilities are shown in Table 2. Of the 72 patients, 30 (42%) had cultures yielding MRSA and 42 (58%) had cultures yielding methicillin-sensitive *S aureus.* Of the 30 patients with MRSA by culture, 28 had a positive nasal PCR, yielding a sensitivity of 93.3%. Of the 42 patients with positive cultures for methicillin-sensitive *S aureus,* 40 had a negative MRSA nasal PCR, yielding a specificity of 95.2%. Twenty-eight of 30 patients with a positive nasal PCR had positive lower respiratory tract cultures for MRSA, giving a positive predictive value of 93.3%. Forty of 42 patients with a negative nasal PCR did not have positive lower respiratory tract cultures for MRSA, giving a negative predictive value of 95.2%.

DISCUSSION

A diagnostic test that correctly guides the discontinuation of empiric MRSA-directed antibiotic therapy must have a low false-negative rate, because a false-negative nasal MRSA PCR test could result in discontinuing MRSA-directed antibiotic therapy in a patient who actually has MRSA lower respiratory tract infection. In other words, we are interested in a test with high sensitivity and negative predictive value. The results of this study show that MRSA nasal PCR screening within 48 hours of admission has high sensitivity, specificity, and positive and negative predictive value for the presence of MRSA in lower respiratory tract culture. Given the low incidence of *S aureus* community-acquired pneumonia (0.8%-3% in well-designed prospective studies),[3,7] the nasal MRSA PCR test, with its high sensitivity and negative predictive value, could be a useful decision-making tool for clinicians to discontinue antibiotic coverage directed against MRSA early in admission. The principal benefits of the PCR screen include the ease of performing the nasal swab and rapid turnaround time. In addition, because respiratory tract samples are often difficult to obtain, the nasal MRSA PCR may be able to inform the discontinuation of MRSA-directed therapy in the absence of a respiratory tract sample.

Our study has several methodologic strengths. Unlike earlier investigators who obtained cultures from sputum and nonrespiratory sites (blood, incisions, and urine),[8] we focused exclusively on the clinically relevant association between *S aureus* colonization of the upper airways, in most cases the presumed source of bacteria that infect the lower respiratory tract, and the presence of MRSA in lower respiratory tract cultures. Secondly, we included only patients with lower respiratory tract cultures obtained within 48 hours of admission, thereby excluding patients with hospital-acquired infections. We also excluded patients transferred from another acute care facility for this reason.

Our study provides compelling data to undertake a more extensive prospective study. Moreover, the findings are consistent with a recent retrospective study in which the MRSA PCR test

Table 2. Calculations of sensitivity, specificity, and positive and negative predictive value for methicillin-resistant *Staphylococcus aureus* nasal polymerase chain reaction test

Parameter	Test performance, percentage (95% CI)
Sensitivity	93.3 (76.9-98.3)
Specificity	95.2 (82.9-98.8)
Positive predictive value	93.3 (76.9-98.3)
Negative predictive value	95.2 (82.9-98.8)

CI = confidence interval.

had a sensitivity of 88% and a negative predictive value of 99.2% in predicting MRSA pneumonia.[9] In contrast to this study, however, our study restricted patients to those with a nasal PCR collected within 48 hours. We selected a cutoff of 48 hours because studies indicate that nasal colonization status changes soon after hospital admission.[10] The literature also suggests that nasal MRSA PCR has decreased sensitivity when clinical culture is obtained long after the PCR test. In a retrospective study of ICU patients by Byrnes et al,[8] the sensitivity of nasal PCR screening for MRSA in clinical cultures was only 69.5%. The sensitivity was most diminished by the inclusion of cultures obtained after 7 days from the initial nasal swab PCR test. In fact, nasal swab PCR screening for MRSA was most sensitive when clinical cultures were obtained within 6 days of the PCR (79% vs 46%, $p < 0.0001$). Furthermore, Sarikonda et al[11] determined that nasal screening with MRSA PCR was a poor predictor (sensitivity 24.2% and negative predictive value 84.4%) of ICU-acquired MRSA lower respiratory tract infections.

This study has certain limitations. We did not include all lower respiratory tract cultures, only those yielding *S aureus.* However, our negative predictive value (ie, the probability that a negative nasal MRSA PCR correctly predicts a negative lower respiratory tract culture for MRSA) can only increase if all positive results of lower respiratory tract cultures were included. Our study was retrospective at a single institution. Given the study's retrospective nature, we do not know the correlation between culture results and lower respiratory tract disease. Because our hospital does not mandate surveillance cultures, presumably physicians ordered lower respiratory tract cultures when they suspected a lower respiratory tract infection. Nevertheless, our findings are still useful because a negative nasal PCR early during admission means that cultures of the lower respiratory tract are exceedingly unlikely (< 5%) to yield MRSA. Even earlier collection of MRSA nasal PCR and respiratory tract culture may improve correlation between tests. In a prospective study, samples could be collected within hours of hospital arrival, and even in the absence of an adequate respiratory tract specimen, PCR might provide data quickly enough to inform antibiotic decision making at admission. Last, because of the small scale of this study, our data are hypothesis generating rather than definitive. Nonetheless, we believe that this study has important implications for antibiotic stewardship. It also provides preliminary data for the conduct of a definitive multicenter prospective clinical study.

CONCLUSION

Nasal PCR for MRSA collected within 48 hours of admission appears to reliably predict the absence of MRSA in lower respiratory tract secretions. This test may have a role in guiding the discontinuation of MRSA-directed empiric antibiotic therapy for patients hospitalized with lower respiratory tract infections. Even though the number of patients in our study is small, the high sensitivity and negative predictive value for MRSA nasal PCR in *S aureus* respiratory tract cultures is certainly suggestive that PCR for MRSA, when collected early in admission, reliably predicts the absence of MRSA in the lower respiratory tract. This warrants further exploration and a prospective study is needed to confirm these findings. ❖

Disclosure Statement

This work was supported in part by the Houston Veterans Affairs Center for Innovations in Quality, Effectiveness and Safety (HFP90-020). The author(s) have no conflicts of interest to disclose.

The views expressed in this article are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs.

Acknowledgments

At the time of this study, Jennifer A Johnson, MD, was a Pulmonary and Critical Care Physician in the Department of Internal Medicine at Baylor University Medical Center; Michael E Wright, PharmD, and Lyndsay A Sheperd, PharmD, were Critical Care Clinical Pharmacists in the Department of Pharmacy at Baylor University Medical Center in Dallas, TX.

Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.

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