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Clinical Studies

Clinical utility of a nasal swab methicillin-resistant *Staphylococcus aureus* polymerase chain reaction test in intensive and intermediate care unit patients with pneumonia

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ABSTRACT

This retrospective study aimed to validate the concordance between nasal swab methicillin-resistant *Staphylococcus aureus* (MRSA) polymerase chain reaction (PCR) test and respiratory culture and to determine the number of potentially preventable days of anti-MRSA therapy in patients with pneumonia. Two hundred adult inpatients in the intensive and intermediate care units were included. The nasal swab MRSA PCR test was positive in 55 (27.5%) patients. MRSA was isolated from respiratory culture in 21 (10.5%) patients. The nasal swab MRSA PCR test demonstrated 90.5% sensitivity, 79.9% specificity, 34.5% positive predictive value, and 98.6% negative predictive value. Anti-MRSA therapy was initiated in 168 (84%) patients. Patients in the study received a combined 782 days of anti-MRSA therapy; 300 days were considered potentially preventable. This study suggests that the nasal swab MRSA PCR test may be used to guide discontinuation of anti-MRSA antibiotics in patients with clinically confirmed pneumonia in the intensive or intermediate care units.

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1. Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of pneumonia, particularly in the intensive care unit (ICU) setting (Chen et al., 2015; Defres et al., 2009; Keene et al., 2005). MRSA is a natural colonizer of the nares, and previous studies have shown that colonization is a risk factor for subsequent infection (Keene et al., 2005; Ridgway et al., 2013; Stenehjem and Rimland, 2013). When pneumonia is suspected, clinicians must determine which patients should receive empiric anti-MRSA therapy and when antimicrobial therapy may be safely de-escalated.

Nasal screening for MRSA colonization has traditionally been used for infection prevention in order to reduce the transmission of this pathogen, as it identifies patients in which to initiate contact isolation precautions and decolonization regimens (Chan et al., 2012; Septimus et al., 2013; Yokoe et al., 2006). Recent studies have also identified a potential use of MRSA nasal screening to guide antimicrobial therapy in patients with suspected pneumonia Chan et al., 2012; Dangerfield et al., 2014; Johnson et al., 2015; Robicsek et al., 2008; Tilahun et al., 2015). These studies have shown that a negative nasal swab has a high negative predictive value (>95%) for ruling out MRSA pneumonia, suggesting that nasal MRSA surveillance may be useful in guiding discontinuation of empiric anti-MRSA antibiotics.

The primary objective of our study was to validate the concordance between the nasal swab MRSA polymerase chain reaction (PCR) test and respiratory culture in ICU and intermediate care unit patients with clinically diagnosed pneumonia in our institution. As a secondary objective of the study, the anti-MRSA antibiotic prescribing patterns in the study population were evaluated to assess the potential days of anti-MRSA therapy that could have possibly been avoided by using a negative nasal swab MRSA PCR test to discontinue anti-MRSA antibiotics.

2. Materials and methods

2.1. Study design and patient population

This was a single-center, retrospective cohort study conducted at St. Mary's Medical Center (SMMC), a 393-bed teaching hospital in Huntington, WV. The Marshall University Institutional Review Board, which reviews all biomedical research involving human subjects at SMMC, approved the study and informed consent was waived. All adult inpatients in the medical, cardiovascular, and neurotrauma ICUs as well as intermediate care units with an admitting diagnosis of pneumonia, respiratory failure, or sepsis between January 1, 2011 and

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September 30, 2015 were screened for enrollment. Additional inclusion criteria included clinically confirmed pneumonia as defined in Section 2.2 and documented results of the nasal swab MRSA PCR test and respiratory culture. During the study period, universal nasal swab MRSA PCR testing was performed for ICU and intermediate care unit patients using the Xpert MRSA Assay in the GeneXpert Dx System (Cepheid, Sunnydale, CA). The SMMC chemistry lab processes the nasal swab upon receipt of the specimen and results are available within two hours. Patients were stratified by pneumonia type to evaluate the clinical utility of the nasal swab MRSA PCR test for community-acquired pneumonia (CAP), healthcare-associated pneumonia (HCAP), and hospital-acquired pneumonia/ventilator-associated pneumonia (HAP/VAP). Based on previous literature, patients were excluded if the nasal swab MRSA PCR test was performed more than 1 month prior to respiratory culture for patients presenting from the outpatient setting, more than 7 days prior to respiratory culture for patients in hospital-acquired cases, or more than 3 days after the respiratory culture was collected (Dangerfield et al., 2014).

2.2. Data collection and definitions

Data were collected from each patient's electronic medical record and included age, sex, pneumonia type, respiratory culture data, and anti-MRSA antibiotic data. Based on the Infectious Diseases Society of America and American Thoracic Society guidelines for community-acquired (2007) and nosocomial pneumonia (2005), clinically confirmed pneumonia was defined as chest X-ray or CT scan with signs of definitive or possible infiltration, consolidation, cavitary lesions, or airspace disease plus at least two of the following signs/symptoms: temperature <36 °C or >38 °C, WBC <4000 or >11,000 cells/mm^3, respiratory rate >20, oxygen saturation <90%, increased cough, increased sputum volume, or sputum purulence (American Thoracic Society and Infectious Diseases Society of America, 2005; Mandell et al., 2007). Patients were classified as having CAP if they presented with pneumonia within 48 hours of admission without any HCAP criteria (Mandell et al., 2007). Patients were considered to have HCAP if they presented with pneumonia within 48 hours of admission and had any of the following criteria: hospitalization for at least two days within the previous 90 days, residence in a nursing home or long-term care facility, received intravenous antibiotic therapy, chemotherapy, or wound care within 30 days, or attended a hemodialysis clinic within 30 days (American Thoracic Society and Infectious Diseases Society of America, 2005). HAP or VAP was defined as onset of pneumonia at least 48 hours after admission or at least 48 hours after endotracheal intubation, respectively (American Thoracic Society and Infectious Diseases Society of America, 2005). The nasal swab MRSA PCR test results were reported as either positive or negative. Sputum cultures were considered MRSA positive if MRSA was isolated in any appreciable degree, as quantitative cultures were rarely performed and a clinically based strategy was used to define pneumonia. Anti-MRSA antibiotics assessed in our study included vancomycin, linezolid, and clindamycin.

2.3. Outcomes/end points

The primary outcome was the concordance between the nasal swab MRSA PCR test and respiratory culture result, which was determined by calculating the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The sensitivity described the probability that the nasal swab MRSA PCR test will be positive among those with MRSA pneumonia and was calculated by dividing the number of true positives (i.e. both nasal swab MRSA PCR test and respiratory culture positive) by the total number of patients with a respiratory culture positive for MRSA. The specificity described the probability that the nasal swab MRSA PCR test will be negative among those without MRSA pneumonia and was calculated by dividing the number of true negatives (i.e. nasal swab MRSA PCR test and respiratory culture negative) by the total number of patients with a respiratory culture negative for MRSA. The PPV described the probability that the patient will have MRSA pneumonia when the nasal swab MRSA PCR test is positive and was calculated by dividing the number of true positives by the total number of patients with a positive nasal swab MRSA PCR test. The NPV described the probability that the patient will not have MRSA pneumonia when the nasal swab MRSA PCR test is negative and was calculated by dividing the number of true negatives by the total number of patients with a negative nasal swab MRSA PCR test. Secondary outcomes included the observed use of anti-MRSA antibiotics and the number of potentially preventable days of anti-MRSA therapy. Days of therapy were rounded to the nearest whole day and were determined by counting each day from the start date through the stop date of the anti-MRSA antibiotics. Potentially preventable days of therapy included all days starting the day after a negative nasal swab MRSA PCR test was obtained through the stop date of the anti-MRSA antibiotics.

3. Results

A total of 562 patients were identified and screened for inclusion; 200 patients were included. The most common reasons for exclusion were no radiographic evidence of pneumonia (n = 201), no nasal swab MRSA PCR test performed (n = 114), and fewer than two signs/symptoms suggestive of pneumonia (n = 29). Patient characteristics are shown in Table 1. As only seven patients were categorized as having HAP/VAP, results were not separately analyzed for this subgroup of patients; however, they were included in the overall analysis.

Respiratory cultures were obtained from endotracheal aspirates (n = 96; 48%), induced sputum specimens (n = 46; 23%), expectorated sputum specimens (n = 33; 16.5%), nasotracheal aspirates (n = 11; 5.5%), bronchial washings (n = 7; 3.5%), and bronchial lavage (n = 6; 3%); the source of respiratory culture was not available for one patient. Twenty-one patients had MRSA isolated from respiratory cultures, resulting in a prevalence of MRSA pneumonia of 10.5%. The prevalence of MRSA CAP and MRSA HCAP was 6.7% and 15.9%, respectively. Among the 21 patients with MRSA isolated, respiratory cultures were obtained from endotracheal aspirates (n = 8), expectorated sputum specimens (n = 5), induced sputum specimens (n = 3), nasotracheal aspirates (n = 2), bronchial washings (n = 2), and bronchial lavage (n = 1). Fifty-five patients had a positive nasal swab MRSA PCR test; 19 of these also had a positive respiratory culture for MRSA. Of the 145 patients that had a negative nasal swab MRSA PCR test, only two had MRSA isolated from respiratory culture; one had CAP and the other had HCAP. The calculated sensitivity, specificity, PPV, and NPV of the nasal swab MRSA PCR test are presented in Table 2.

Anti-MRSA therapy was initiated in 168 patients (84%), including 78 patients (74.2%) with CAP, 84 patients (95.5%) with HCAP, and 6 patients (85.7%) with HAP/VAP; the majority received vancomycin (95.2%). Other anti-MRSA agents used included linezolid and

Table 1
Patient characteristics (n = 200).

	No. (%) of patients
Male	107 (53.5)
Age, median (range)	66 (24–94)
Pneumonia Type	
CAP	105 (52.5)
HCAP	88 (44)
HAP/VAP	7 (3.5)
Positive nasal swab MRSA PCR test	55 (27.5)
MRSA-positive respiratory culture	21 (10.5)
Anti-MRSA therapy	168 (84)

CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia; HAP/VAP, hospital-acquired pneumonia/ventilator-associated pneumonia; MRSA, methicillin-resistant *Staphylococcus aureus*; PCR, polymerase chain reaction.