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Concise Communication

Association between a rapid diagnostic test to detect methicillin-resistant *Staphylococcus Aureus* pneumonia and decreased vancomycin use in a medical intensive care unit over a 30-month period

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Abstract

Vancomycin overuse is common, yet few data are available regarding how to improve stewardship of this antibiotic. We identify an association between use of a PCR assay to rule out MRSA pneumonia and a significant, sustained decrease in average vancomycin days of therapy over a 30-month period.

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Methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia is associated with substantial morbidity and mortality, prompting clinicians to include an anti-MRSA antibiotic in the empirical treatment of critically ill patients with suspected pneumonia.[1] A recent multicenter cohort study concluded that empirical anti-MRSA therapy in patients with pneumonia was not associated with a reduction in 30-day mortality.[2] A second study in patients with MRSA bacteremia randomized to standard of care versus combination therapy with vancomycin or daptomycin was stopped early due to increased incidence of acute kidney injury in patients treated with anti-MRSA therapy.[3] These studies, along with others, suggest that anti-MRSA antibiotics may be used more often than indicated and without a clear benefit. However, few published data demonstrate how to effectively reduce anti-MRSA antibiotic use, especially in the critically ill population.

We previously performed a clinical trial randomizing intubated patients with suspected pneumonia to standard care versus antibiotic management based on the result of a rapid polymerase chain reaction assay (RPCR) that detects the *mec*A gene which confers methicillin resistance to *S. aureus*.[4] This clinical trial was performed from May 2016 to January 2017 and consisted of a total of 45 patients; 22 were randomized to PCR-guided antibiotic management and 23 were randomized to usual care. The PCR assay used in the clinical trial was the MRSA/SA SSTI kit on the Cepheid GeneXpert platform, which identifies DNA sequences for *Staphylococcus aureus* and for methicillin/oxacillin resistance (mecA). This RPCR was performed on nonbronchoscopic bronchoalveolar lavage (NBBAL) and bronchoscopic alveolar lavage (BAL) samples. In this study, the protocol directed clinicians to discontinue anti-MRSA antibiotics if the RPCR result was negative. We demonstrated a significant decrease in the duration of anti-MRSA antibiotic administration in the intervention group compared to the control group, without an increase in adverse events.

Following this study, our institution made the RPCR test available for clinicians to order on NBBAL and BAL samples. We also implemented an 8-month quality improvement project to provide clinicians with education on use and interpretation of the RPCR test. In this report, we examine trends in vancomycin use in the 2 years following the implementation the RPCR test in our medical intensive care unit (MICU).

Methods

This study was performed at Northwestern Memorial Hospital (NMH) in Chicago, Illinois. We received approval from our institutional review board (no. STU00202148). Data on hospital-wide vancomycin use at NMH is collected from the electronic medical record (EMR) and bar code medication administration data on a regular basis and submitted to the National Healthcare Safety Network. We accessed this data from January 2015 to December 2019 specifically for vancomycin use in the medical intensive care unit (MICU). Vancomycin use was measured as days of therapy (DOT) per 1,000 days present in the MICU. The RPCR for MRSA was made available as an order in the EMR in June 2017. We extracted the number of RPCRs for MRSA ordered each month in our 31-bed MICU from the EMR. Correlation between

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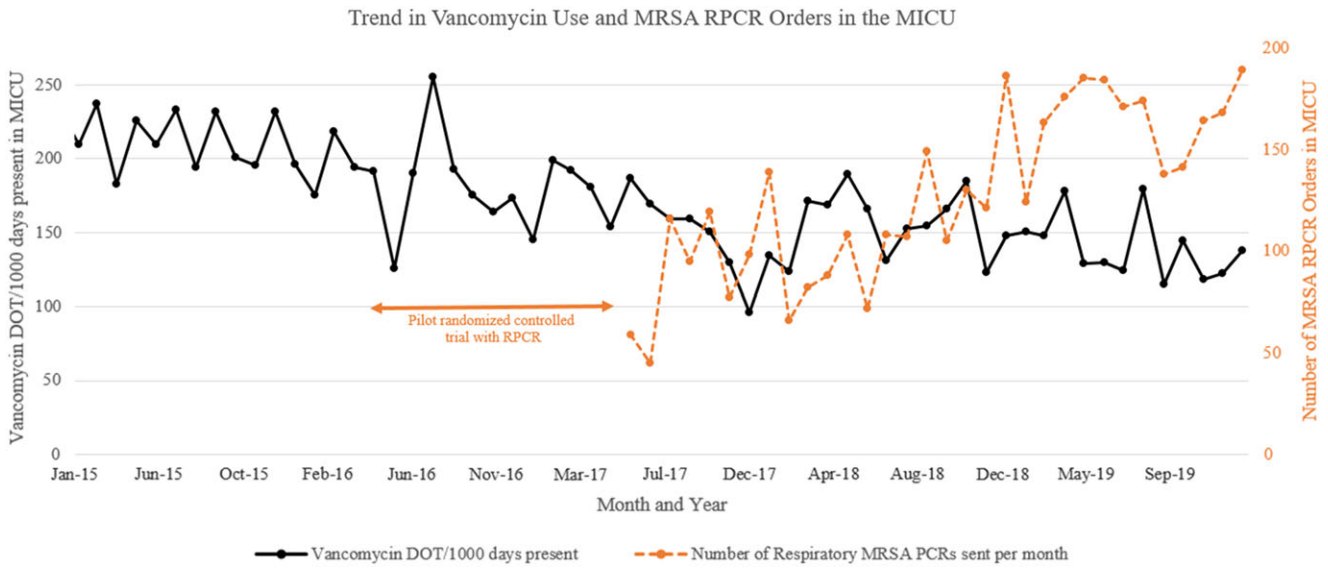

Figure 1. Trend in vancomycin use versus number of MRSA RPCR orders in the medical intensive care unit.

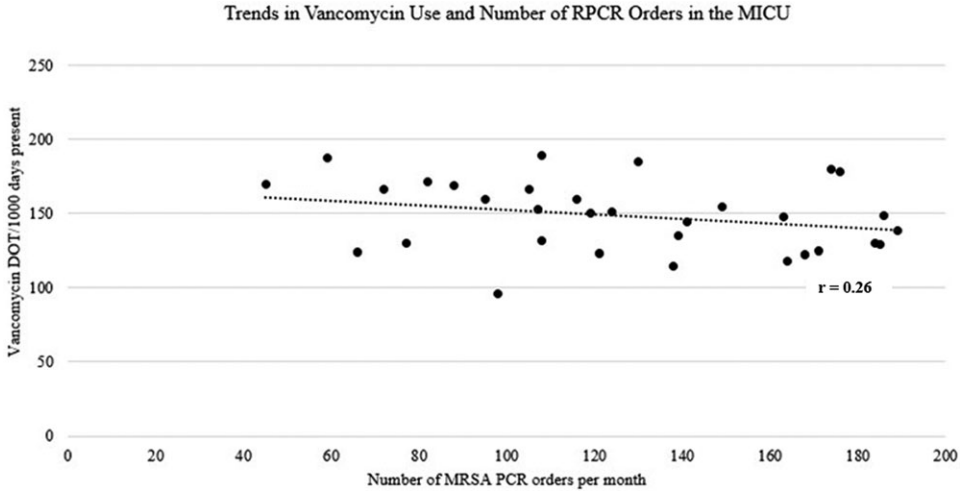

Figure 2. Trends in vancomycin use based on number of RPCR orders in the medical intensive care unit.

vancomycin DOT per 1,000 days present and the number of RPCRs ordered was determined by calculating the mean monthly vancomycin use and plotting this as the dependent variable versus the independent variable, which was number of RPCR tests.

Results

Vancomycin use decreased from 2015 to present, with a sharper decline following the clinical trial and implementation of the RPCR in the MICU (Fig. 1). Mean vancomycin DOT per 1,000 days present before RPCR implementation (January 2015 to May 2017) was 197. Mean use after RPCR implementation (June 2017 to December 2019) was 148. The mean difference of 49 DOT per 1,000 days present was significant by 2-sided *t* test ($P = .001$). When the period during which the initial clinical trial was performed was excluded from the analysis, the difference in vancomycin use before and after RPCR implementation remained significant (210 DOT per 1,000 days present vs 151 DOT per 1,000 days present; $P < .001$). In the post-RPCR implementation period, the number of RPCR orders per month and vancomycin therapy per month were not correlated (Fig. 2). Notably, linezolid use in the MICU was not significantly different. From September 2015 to May 2017, mean linezolid used was 51.2 DOT per 1,000 days present and from June 2017 to December 2019 mean linezolid used was 53.2 DOT per 1,000 days present ($P = .691$).

Discussion

In this single-center report, we have demonstrated a significant association between use of a MRSA RPCR and decreased vancomycin use in the MICU. Despite this, we detected no direct relationship between low versus high numbers of RPCR orders and vancomycin use.

We suspect that a significant proportion of vancomycin use is for empiric therapy for suspected MRSA pneumonia rather than for other MRSA infections. Thus, our efforts to focus on vancomycin use in pneumonia made a significant impact on total vancomycin use. Previous studies have demonstrated that rapid diagnostic

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tests are more effective when coupled with antibiotic stewardship programs.[5] We believe that the introduction of the MRSA RPCR test was associated with decreased vancomycin use because our MICU clinicians were also provided with guidance and education during the initial 8 months of RPCR implementation. Also, after several uses of the RPCR, clinicians may have learned when to suspect or not suspect MRSA pneumonia without relying on the RPCR result to guide antibiotic decisions.

This study has several limitations. Knowledge of the prior clinical trial of RPCR use in our MICU may have biased clinicians to be more willing to de-escalate antibiotics based on a negative RPCR result. Additionally, this is a single-center study in a MICU which limits generalization to other ICUs and hospitals, particularly in settings in which NBBAL and BALs are not routinely performed for suspected pneumonia on intubated patients. However, given the consistent evidence that anti-MRSA therapy is associated with acute kidney injury without proven mortality benefit, reduction of unnecessary use of these antibiotics is important. Our study offers a practical and sustainable method for decreasing vancomycin use in a vulnerable patient population.

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Conflicts of interest. R.G.W. is a consultant for bioMerieux and Accelerate Diagnostics. His institution has received research grants from bioMerieux and Curetis. All other authors declare no conflict of interest and have no financial disclosures to report.

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