Patients and Clinical Outcomes. The 5-year surveillance study has been ongoing since 2001; patients are prospectively enrolled in seven of the participating healthcare-associated (HCA) MRSA bacteremia inpatient admission records. Enrollment included any patient admitted to non-ICU wards with healthcare-associated MRSA bacteremia. Exclusions: In order to minimize the impact of prior exposure to clinical outcomes, patients were excluded who had an isolated viridans streptococcus bacteremia, or whose isolates were identified as vancomycin-resistant enterococcus. Duration of bacteremia was defined by the number of viable days between the last prior blood culture with positive isolate to the resolution of the previous infection. To calculate vancomycin MICs used in the analysis above, vancomycin was determined with the use of E-test. The highest vancomycin serum trough observed on any given day and during the duration of bacteremia. The phenotype of vancomycin resistance ≤ 0.5 µg/ml was associated with a greater risk of AKI (odds ratio (OR) 6.01; 95% confidence interval (CI) 2.2 to 16.5). Multivariate analysis was performed with the use of the multivariate logistic regression model.

The Impact of Acute Kidney Injury on Outcomes. The multivariate analysis was not statistically significant due to underpowered studies.

Nosocomial And Community-Onset Healthcare Associated MRSA Bacteremia in Children: Evidence for “Reverse Vancomycin Creep” and Limited Benefit of Elevated Vancomycin Serum Troughs

J. Chase McNeil, MD, Linda Lambeth, MS, Eric Kok, Kristina G. Hultén, PhD, Sheldon L. Kaplan, MD and Edward O. Mason, PhD

Department of Pediatrics, Section of Infectious Diseases, Baylor College of Medicine and Texas Children’s Hospital, Houston, Texas

ABSTRACT

Background. Vancomycin is the most commonly used drug for the treatment of serious infections in children. Vancomycin serum troughs have been used in an effort to optimize vancomycin concentrations, however, there is limited data on the safety of elevated vancomycin troughs, especially in children with severe infections.

Aim. To evaluate the impact of elevated vancomycin serum troughs on outcome in healthcare-associated MRSA bacteremia.

Patients and Methods. The study was a prospective, single institutional clinical cohort study of patients admitted with healthcare-associated MRSA bacteremia from 2008-2012. Patients were identified from a prospectively entered surveillance database. Vancomycin MICs were determined by Etest. Medical records were reviewed. An isolate was considered an MRSA only if it was fully susceptible to vancomycin. Results: During the study period from May 2008 to December 2013, 250 children were identified with healthcare-associated MRSA bacteremia. 54 (57.4%) of isolates were not susceptible to vancomycin with MICs of 0.5 µg/ml, 2.0 µg/ml, and ≥2.0 µg/ml. The median MIC was 1.5 µg/ml. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age.

Table 1. Characteristics of Patients and Isolates

Table 2. Comparison of Patients With And Without Acute Kidney Injury

Table 3. Comparison of Treatments With And Without Acute Kidney Injury

Table 4. Multivariate Analysis of Risks For Acute Kidney Injury

Introduction

Vancomycin remains the antibiotic of choice for MRSA infections in children.

While the majority of isolates are susceptible by broth microdilution and automated methods, a number of isolates have shown trends towards clinical resistance in association with vancomycin E-test minimum inhibitory concentration (MIC) of 1 µg/ml (Lodise et al. Clin Microbiol Infect 2012; 18: 20-6). Work in adults has suggested that vancomycin E-test MIC for MRSA has increased slightly over time. In J. Am. Med. Assoc. JAMA 2008; 299: 1-10 it was demonstrated that vancomycin MIC ≥1 µg/ml is associated with a “reverse vancomycin creep” phenomenon.

Studies suggesting that vancomycin creep may be occurring in children may not be consistent with recent results (Masoli ED. J Clin Microbiol 2009; 47: 1828-30). Earlier studies have failed to show that vancomycin MIC of 1 µg/ml is associated with a “reverse vancomycin creep” phenomenon.

The Infectious Diseases Society of America recommends targeting vancomycin dosing with both intra- and inter-study MICs of ≥15 µg/ml for severe MRSA infections including vancomycin-resistant enterococcus (Liu CL. Infect Dis Clin N Am. 2011; 55: 123-31).

These high trough concentrations are often difficult to achieve in children (Chen JP. Pediatr Infect Dis J. 2007; 26: 992-8). Furthermore the appropriate trough concentration in order to achieve optimal AM/CMI ratio in children is unknown (Frymoyer et al. Pediatr Infect Dis J. 2003; 22: 825-30).

Methods: Isolates and patient records with nosocomial and community-onset healthcare-associated MRSA bacteremia from 2008-2012 were identified from a prospective surveillance database. Vancomycin MICs were determined by Etest. Medical records were reviewed. An isolate was considered an MRSA only if it was fully susceptible to vancomycin. Results: During the study period from May 2008 to December 2013, 250 children were identified with healthcare-associated MRSA bacteremia. 54 (57.4%) of isolates were not susceptible to vancomycin with MICs of 0.5 µg/ml, 2.0 µg/ml, and ≥2.0 µg/ml. The median MIC was 1.5 µg/ml. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age. AKI was defined as a rise in serum creatinine of >1.5 mg/dL in children ≤ 5 years of age and >2.0 mg/dL in children >5 years of age.

Conclusion: Vancomycin MIC of ≥15 µg/ml was associated with a shorter duration of bacteremia compared to those with MIC ≤1.5 µg/ml. Given that most vancomycin MICs did not exceed 1 µg/ml, this study likely underestimates a benefit of elevated troughs. Elevated vancomycin troughs are, however, clearly associated with a risk for acute kidney injury.

Further multicenter prospective studies are needed to better understand optimal vancomycin dosing in children.