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ORIGINAL ARTICLE

Methicillin-resistant *Staphylococcus aureus* bacteremia in hemodialysis and nondialysis patients

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Bacteremia;
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Minimum inhibitory concentration

Background/Purpose: Increased mortality has been reported in patients treated with vancomycin for methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia with high minimum inhibitory concentration (MIC) values within the susceptibility range. However, this finding has not been verified in hemodialysis patients, who have much higher invasive MRSA infection rates than nondialysis patients. We aimed at comparing vancomycin MICs between hemodialysis and nondialysis patients, and identifying predictors of high vancomycin MICs and infection-related mortality in hemodialysis patients with MRSA bacteremia.
Methods: Patients with MRSA bacteremia from January 2008 through December 2009 were enrolled. Vancomycin MIC was determined for each first isolate using the Etest method. Clinical characteristics and vancomycin MICs were compared between hemodialysis and nondialysis patients. Factors associated with high vancomycin MIC (2 μg/mL) and infection-related mortality in hemodialysis patients were analyzed.
Results: A total of 162 MRSA bacteremia episodes were identified. Forty-four (27.0%) isolates were obtained from hemodialysis patients and 118 (73.0%) from nondialysis patients. Diabetes (63.3% vs. 39.8%, $p = 0.007$) and prior vancomycin exposure in 30 days (31.8% vs. 12.7%, $p = 0.005$) were more prevalent in hemodialysis group than in nondialysis group. A higher

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prevalence of vancomycin MIC of 2 μg/mL was observed in hemodialysis group in comparison with nondialysis group (11.4% vs. 1.7%, $p = 0.016$). In following analyses of hemodialysis group, patients with initial presentation of septic shock had a higher risk of vancomycin MIC of 2 μg/mL than nonseptic shock patients (100.0% vs. 38.5% $p = 0.014$). Infection-related mortality was associated with age, Acute Physiology and Chronic Health Evaluation II (APACHE-II) score >15, presence of septic shock, receipt of mechanical ventilation, and failure to remove source of bacteremia in univariate analysis.

Conclusion: Hemodialysis patients with MRSA bacteremia are more likely to have a high vancomycin MIC (2 μg/mL) compared with nondialysis patients. Infection-related mortality is associated with the patient's clinical manifestations, including age, APACHE-II score >15, presence of septic shock, receipt of mechanical ventilation, and failure to remove source of bacteremia. Treatment selection should be tailored according to the patient's clinical condition.

Introduction

Staphylococcus aureus is the most common pathogen of bloodstream infections (BSIs) in hemodialysis patients.[1,2] In 2005, invasive methicillin-resistant *S. aureus* (MRSA) infections occurred in 45.2/1000 dialysis patients, a rate more than 100 times higher than in nondialysis patients.[3] Patients with MRSA bacteremia who are undergoing hemodialysis have a five-fold higher risk for death and >100% higher hospital costs than uninfected patients undergoing hemodialysis.[4]

Vancomycin is one of the most commonly administered antimicrobial agents in hemodialysis patients, because of both high risk of systemic MRSA infections and ease of administration.[5] Despite its sustained *in vitro* microbiological inhibitory activities, emerging data suggest that vancomycin may be less effective against MRSA infections with minimum inhibitory concentrations (MICs) at the higher end of the susceptibility range.[6] Patients undergoing hemodialysis with MRSA bacteremia had been studied in the United States,[7] but no local data are available in Taiwan. We conducted this study to identify and compare the clinical characteristics and vancomycin MICs between hemodialysis and nondialysis patients with MRSA bacteremia. Factors associated with high vancomycin MIC and infection-related mortality in hemodialysis group were analyzed.

Materials and methods

Study design and patients

This retrospective study was conducted at Tri-Service General Hospital, a 1700-bed primary care and tertiary referral center in northern Taiwan. A list of patients with MRSA bacteremia from January 2008 through December 2009 was retrieved from the hospital's clinical microbiology laboratory database. The patients were divided into two groups. Hemodialysis group comprised all patients who had undergone hemodialysis for more than 3 months prior to enrollment; the remaining patients were classified as nondialysis group. Demographic data, comorbidities, Charlson Comorbidity Index, Acute Physiology and Chronic Health Evaluation II (APACHE-II) score, initial presentation of septic shock, surgery within 30 days, vancomycin exposure within 30 days, receipt of mechanical ventilation, use of vascular access device, vancomycin MICs, and infection-related mortality were retrospectively collected for all patients. Additionally, causes of hemodialysis, source of bacteremia, removal of source of bacteremia, administration of empirical antimicrobial agents, presence of persistent bacteremia, and mortality rate within 14 and 28 days after onset of bacteremia were analyzed in hemodialysis group.

Definition

MRSA bacteremia was defined as the presence of at least one set of blood culture yielding MRSA. Comorbidities were defined as diseases that cause functional impairment and/or predispose patients to infection, such as alcoholism (consumption of >100 g of alcohol per day), chronic obstructive pulmonary disease, dementia, diabetes, heart failure, hematological neoplasms, immunosuppressive therapy (>10 mg of prednisolone daily within 4 weeks, or other agents used as antineoplastic chemotherapy or to prevent organ rejection), liver cirrhosis, solid neoplasms, and valvular heart disease. Causes of hemodialysis were identified by either renal biopsy pathology report or medical record. Septic shock was diagnosed on the basis of standard clinical definition.[8] Hospital-onset BSI was defined as bacteremia occurring >48 hours after hospital admission. Surgery within 30 days was defined as operation under either general or local anesthesia in the past 30 days. All catheters used at onset of bacteremia were recorded. Tunneled catheters were passed under the skin from the insertion site to a separate exit site, where the catheter and its attachments emerge from underneath the skin (Por-A-Cath or double lumen catheter, for instance). Any dose of vancomycin exposure within 30 days was analyzed. Persistent bacteremia was defined as growth of MRSA with identical antibiogram on Day 7 or after, within 30 days of the first positive blood culture. Infection-related mortality was defined as death occurred (1) within 7 days after positive blood cultures or (2) prior to resolution of signs and symptoms of MRSA bacteremia or (3) 7 days after the onset of MRSA bacteremia without any obvious cause other than bacteremia.