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VANCOMYCIN USE IN PATIENTS DISCHARGED FROM THE EMERGENCY DEPARTMENT: A RETROSPECTIVE OBSERVATIONAL COHORT STUDY

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☐ **Abstract—Background: Infections due to methicillin-resistant *Staphylococcus aureus* (MRSA) are associated with significant morbidity and mortality and are typically treated with intravenous vancomycin. Given vancomycin's time-dependent mechanism of action, it is unlikely that vancomycin administration in the emergency department (ED) prior to disposition home could be beneficial. Study Objectives: To characterize the indications, dosing, and appropriateness of vancomycin use in patients discharged from the ED. Methods: This is a single-center retrospective observational cohort study of patients who received vancomycin in an urban, academic, tertiary care ED. The subjects were consecutive adult patients administered intravenous vancomycin in the ED and then discharged home over an 18-month period. Outcomes were measured 1) to characterize patients receiving vancomycin prior to discharge home from the ED; and 2) to identify patients that did not meet indications for appropriate use based on the 2011 Infectious Diseases Society of America guidelines for treating MRSA infections. Results: There were 526 patients that received vancomycin in the ED prior to discharge during the study period. In this cohort, 368 (70%) patients were diagnosed with skin and soft tissue infections. A MRSA risk factor was present in 396 (75%) patients. Prior to discharge, one dose of vancomycin was administered to 357 (68%) patients. Underdosing of vancomycin occurred in 239 (73%) patients. Conclusions: Vancomycin was given frequently to patients discharged home from the ED, most commonly for conditions where vancomycin was not indicated, such as skin and soft tissue infections. The majority of these patients received a vancomycin dosing strategy that is not only unlikely to lead to clinical improvement, but also has the potential to contribute adversely to the development of antibiotic resistance. Further investigation is needed into the impact of vancomycin use, the emergence of vancomycin resistance, and the role of ED-based antibiotic stewardship.** © **2015 Elsevier Inc.**

☐ **Keywords—antibiotic stewardship; emergency department; methicillin-resistant *Staphylococcus aureus* (MRSA); skin and soft tissue infection (SSTI); vancomycin**

INTRODUCTION

Antibiotic resistance is a major public health concern, and is developing at a rate that outpaces new antimicrobial therapies (1,2). The emergence of multidrug-resistant (MDR) pathogens is frequently related to inappropriate antimicrobial therapy, and is associated with worse outcomes in a variety of infectious conditions (3–9). Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major problem in both community and in-hospital settings, and causes significant morbidity, mortality, and financial burden in the United States (10–15). Additionally, the emergence of vancomycin-intermediate *Staphylococcus*

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aureus (VISA) and vancomycin-resistant *Staphylococcus aureus* (VRSA) is invariably associated with previous vancomycin exposure and threatens the efficacy of vancomycin in the treatment of severe MRSA infections (16–22).

There is an increased interest in the potential role of the emergency department (ED) in antibiotic stewardship (23,24). It is appropriate to administer vancomycin in the setting of a known or suspected MRSA infection, or in the setting of a severe systemic illness with a high risk of mortality (6,22,25). In 2011, the Infectious Diseases Society of America (ISDA) specifically recommended the use of vancomycin in complicated skin and soft tissue infections (SSTI), bacteremia, infective endocarditis, pneumonia, osteomyelitis, septic arthritis, meningitis, and intracranial abscesses (26). Our previous work indicates that vancomycin is commonly administered in the ED, but that the correct weight-based dose was given in the ED only 22% of the time, and that the majority of patients (83.8%) were given an inpatient dose of vancomycin unchanged from the dose administered in the ED (27). Vancomycin use in patients discharged from the ED has not been studied, however. The bactericidal activity of vancomycin utilizes a time-dependent mechanism of action (22,28). Increased mean inhibitory concentration of vancomycin needed to treat MRSA infections is a mechanism of action of VISA (29). For this reason, a single-use dosing scheme is unlikely to yield significant clinical improvement prior to discharge home from the ED, and may be a patient safety issue with respect to the development of MDR pathogens and unnecessary drug exposure. For example, prior in vitro work indicates that any exposure to vancomycin in the previous 30 days increases the mean inhibitory concentration of vancomycin needed to treat MRSA, potentially leading to the development of VISA (19).

We therefore decided to investigate vancomycin use in patients discharged from the ED. This study was designed to achieve the following objectives: 1) to characterize patients receiving vancomycin prior to discharge home from the ED; and 2) to identify patients that did not meet indications for appropriate use based on the 2011 ISDA guidelines for treating MRSA infections (26). Based on the known pharmacokinetic properties of vancomycin, ISDA guidelines, and our previous work on vancomycin dosing in the ED, we hypothesized that vancomycin administration would be common in patients discharged from the ED, and inappropriate based on indication and dosing strategy.

METHODS

This analysis was a single-center, retrospective, observational cohort study conducted in the ED of an urban, academic, tertiary care institution with an annual census of > 90,000 patients. This observational study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies (30). The subjects were consecutive adult patients administered intravenous vancomycin in the ED and then discharged home over an 18-month period (December 2008 to June 2010). The protocol was approved by the Human Research Protection Office at the principal investigator's institution.

Data were collected on patients identified by query of the ED electronic medical record. The medical record was queried for all patients who received intravenous (i.v.) vancomycin in the ED and were subsequently discharged home during the study period. Variables were defined prior to data extraction and placed in a standardized format during the data collection process. All data were collected by the principal investigator and cross-checked for accuracy prior to data analysis.

Data included patient demographics, chief complaint, diagnosis, dose of vancomycin administered in the ED, other antibiotics administered in the ED, antibiotics prescribed on discharge home from the ED, MRSA risk factors, and appropriateness of vancomycin use. In accordance with the 2011 ISDA guidelines for the treatment of MRSA, we defined appropriate use as vancomycin used in complicated SSTIs, bacteremia, infective endocarditis, pneumonia, osteomyelitis, septic arthritis, meningitis, and intracranial abscesses (26). For the purposes of this retrospective study, patients who presented with SSTI and were subsequently discharged home were defined as not having a complicated SSTI, with the assumption that complicated SSTIs would be admitted for further management and treatment. We defined the "correct" dose of vancomycin as 15–20 mg/kg of the actual body weight based on guideline recommendations (22). MRSA risk factors considered appropriate for empiric i.v. vancomycin therapy included the following, as identified in a recent multicenter investigation in the ED setting: diagnosis of abscess, antibiotic use in the last 30 days, reported spider or insect bite, a personal history of MRSA, and close contacts with a similar infection (25). SSTIs were defined as an ED diagnosis of abscess, abscess plus cellulitis, or cellulitis. Outcomes of interest included subsequent return to the ED with the same medical complaint or need for admission for the same medical complaint, and resolution of symptoms by follow-up office or ED visit. All outcomes of interest were assessed for the 12-month period after the initial ED visit.

Descriptive statistics were used to further characterize these data. The data were generated using SAS software, version 9.1of the SAS System for Linux (SAS Institute Inc., Cary, NC). Statistical analysis was completed in consultation with a biostatistician.