Diagnostic Microbiology and Infectious Disease 82 (2015) 215–221

Contents lists available at ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio

Increased antimicrobial susceptibility rates for *Pseudomonas aeruginosa* bloodstream isolates across the Veterans Affairs Healthcare System ☆

Chris A. Gentry [a,*], Riley J. Williams II [a]

[a] Oklahoma City VA Medical Center, Pharmacy Service (119), 921 NE 13th Street, Oklahoma City, OK 73104

ARTICLE INFO

Article history:
Received 10 July 2014
Received in revised form 11 March 2015
Accepted 22 March 2015
Available online 9 April 2015

Keywords:
Pseudomonas aeruginosa
Susceptibility
Surveillance

ABSTRACT

This study sought to characterize the trends in antimicrobial susceptibility rates for *Pseudomonas aeruginosa* causing bacteremias across the US Veterans Healthcare Administration from 2007 through 2013 utilizing a national clinical database. Data were gathered from 107 Veterans Affairs medical centers involving 4418 patients with 4826 blood cultures with positive growth of *P. aeruginosa*. Susceptibility rates of β-lactam antimicrobials, carbapenems, fluoroquinolones, and aminoglycosides all significantly increased throughout the 7-year period, closely corresponding to a significant decline in the incidence of *P. aeruginosa* blood cultures of nosocomial origin. Several statistically significant increases in susceptibility rates were found for antimicrobial agents across different geographic regions of the United States. There were no statistically significant decreases in susceptibility rates for any antimicrobial agents for any region. Levels of multidrug resistance significantly declined throughout the study period in 2 regions and increased in 1. Additional efforts should evaluate variables associated with these improvements.

Published by Elsevier Inc.

1. Introduction

Healthcare systems struggle to contain the growing problems of healthcare-associated infection (HAI) and antimicrobial resistance (Sievert et al., 2013; WHO, 2001). One organism in particular, *Pseudomonas aeruginosa*, is notorious for its ability to cause serious infections and become resistant to multiple antimicrobial agents (Kallen et al., 2010; Master et al., 2011; Obritsch et al., 2004; Tam et al., 2010; Wisplinghoff et al., 2004). *P. aeruginosa* is a leading cause of Gram-negative bacilli bacteremia and is associated with high mortality rates (Fagan et al., 2013; Kang et al., 2003; Lodise et al., 2007; Micek et al., 2005; Osih et al., 2007; Vidal et al., 1996; Wisplinghoff et al., 2004). Several antimicrobial susceptibility surveillance reports indicate that the level of resistance of *P. aeruginosa* to various antimicrobial agents has significantly increased in the past several years (Jones et al., 2009; Master et al., 2011; Obritsch et al., 2004; Rhomberg and Jones, 2009).

The Veterans Health Administration (VHA) is the largest integrated healthcare system in the United States, consisting of 132 acute care medical centers and 820 community-based outpatient clinics, with approximately 9 million veterans enrolled and over 6 million treated in 2013 (United States Department of Veterans Affairs National Center for Veterans Analysis and Statistics, 2014). The VHA maintains the Corporate Data Warehouse (CDW), a central clinical and administrative relational database containing information from individual Veterans Affairs (VA) medical centers (VAMCs). Recently, bacteriology and susceptibility data became available in the CDW. Because of the dual threat of serious infections and challenging resistance tendencies, the current study sought to utilize the CDW to characterize trends in antimicrobial susceptibility rates for *P. aeruginosa* causing bacteremias across the VHA healthcare system from 2007 through 2013.

2. Materials and methods

2.1. Data collection

Antimicrobial susceptibility results from blood cultures growing *P. aeruginosa* were examined for patients admitted to a VAMC from a period of January 2007 through December 2013. The VHA CDW was utilized to retrieve all of the data. Researchers, upon obtaining approval through a rigorous information security process, log onto the VHA Informatics and Computing Infrastructure (VINCI) workspace via their office computer on the VHA intranet through a secure gateway to access data from the CDW. The protocol was approved by the University of Oklahoma Health Sciences Center Institutional Review Board (IRB protocol no. 3818) and the Oklahoma City Research and Development Committee. In addition, approval for access to VHA CDW data and the VINCI workspace was sought and obtained through the VHA Office of Director, National Data Systems. Data collection included date of culture, facility, facility demographics, antimicrobial MICs and sensitivity interpretations, patient scrambled (deidentified) social security number, and patient admission and discharge dates. Facility data were aggregated to the US Census Bureau regions to

☆ Previous publications: Portions of this work were presented at the September 2014 Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, DC.

* Corresponding author. Tel.: +1-405-456-1549; fax: +1-405-456-5934.
E-mail address: chris.gentry@va.gov (C.A. Gentry).

http://dx.doi.org/10.1016/j.diagmicrobio.2015.03.020
0732-8893/Published by Elsevier Inc.

which they belonged, as well as their respective VAMC facility complexity level model group (Szabo, 2005). Facility complexity levels are determined by characteristics of the patient population, clinical services offered, educational and research missions, and administrative complexity. Level 1 represents the most complex facilities, level 2 represents moderately complex facilities, and level 3 represents the least complex facilities. Level 1 is further divided, primarily reflecting size of the patient population served by the facility into large facilities (1a), moderately large facilities (1b), and small facilities (1c). Blood cultures were determined to be collected as nonnosocomial specimens or nosocomial specimens by comparison of the date of the blood culture specimen and the patient's admission date; specimens were deemed nosocomial if they were procured >48 hours into a patient's hospital admission. Any positive blood culture received from and processed by a VA facility clinical microbiology laboratory was included, regardless of location (ie, emergency room, inpatient ward, outpatient clinic, and affiliated VHA long-term care facility) from which the blood culture was drawn. Duplicate cultures, defined as those taken within 30 days of a previous positive culture, were excluded from analysis. Bed days of care were drawn from national VHA online facility data (VHA Support Services Center, http://vssc.med.va.gov/), and only bed days from acute medical and surgical wards were used in calculations.

2.2. Susceptibility testing

Of the 107 VA facility laboratories from included sites, all were contacted to determine the equipment used during the study period; 63 (58.9%) facility laboratories used a Vitek® System (bioMerieux, Durham, NC, USA), 39 (36.4%) employed Microscan® Microbiology Systems (Siemens Healthcare, Malvern, PA, USA), 3 (2.8%) used BD Phoenix™ Microbiology Systems (Becton Dickinson and Company, Franklin Lakes, NJ, USA), and 2 (1.9%) facilities sent out samples to commercial reference laboratories (personal communication). The clinical microbiology laboratories of each facility are required to maintain compliance and achieve certification with the Centers for Medicare & Medicaid Services Clinical Laboratory Improvement Amendments. Laboratories use susceptibility testing equipment approved by the US Food and Drug Administration. Organism identification and susceptibility testing methods were conducted according to recommendations established by the Clinical and Laboratory Standards Institute (CLSI), and CLSI interpretive MIC breakpoint criteria were applied for determination of susceptibility rates. Some facilities only enter the susceptibility interpretation (ie, susceptible, intermediate, or resistant) in the 2 data fields available for extraction. Other facilities enter the MIC and the susceptibility interpretation into these fields. Importantly, there was no evidence (from examining MIC breakpoint determinations among the various facilities, every isolate with a piperacillin-tazobactam MIC of 32–64 μg/mL was reported as susceptible, and every isolate with an imipenem or meropenem MIC of 2–4 μg/mL was reported as susceptible) that any laboratories were able to utilize the revised MIC breakpoints recommended by CLSI from 2009 through 2011 for certain β-lactam and carbapenem antibiotics against *P. aeruginosa*, presumably due to the widely recognized delay in availability of revised software and equipment. Therefore, susceptibility rates in this study reflect the CLSI MIC breakpoint standards that predated any of the recent lowered MIC breakpoints. For the purposes of this study, an antimicrobial agent displaying intermediate susceptibility according to the CLSI guidelines to a *P. aeruginosa* strain was considered resistant. The following antimicrobial agent's susceptibility results were collected and analyzed: aztreonam, cefepime, ceftazidime, piperacillin-tazobactam, imipenem, meropenem, ciprofloxacin, levofloxacin, gentamicin, tobramycin, and amikacin. For the pairs cefepime and ceftazidime, imipenem and meropenem, and ciprofloxacin and levofloxacin, significant overlap was expected to occur as facilities either test both agents or select 1 of the 2 agents to test on their susceptibility panels. For this reason, the susceptibility result of the most commonly selected single agent (ceftazidime, imipenem, and ciprofloxacin) was the lone agent included in facilities that tested and reported both agents of each pair to avoid duplication when stratifying results by year, region, or nosocomial origin.

Multidrug resistance (MDR) was assessed by year, region, and facility complexity level. MDR was defined as the organism having resistance to all antibiotics tested among at least 3 different classes. In this study, 4 antimicrobial classes were defined as the β-lactam/monobactams (piperacillin-tazobactam, ceftazidime, cefepime, and aztreonam), carbapenems (imipenem and meropenem), fluoroquinolones (ciprofloxacin and levofloxacin), and aminoglycosides (gentamicin, tobramycin, and amikacin).

2.3. Statistical analysis

Statistical analysis was conducted using JMP Pro 10 (SAS Institute, Cary, NC). Categorical data were assessed by using χ^2 or Fisher's exact test. The a priori alpha for all statistical analyses was set at $P < 0.05$.

3. Results

3.1. Characteristics of the clinical isolates

P. aeruginosa was obtained from 4826 blood cultures taken from 4418 patients across 107 VAMCs during the study period. Data from 25 VAMCs were not available in the CDW. The number of *P. aeruginosa* bacteremias declined throughout the study period: 768 in 2007, 794 in 2008, 723 in 2009, 686 in 2010, 656 in 2011, 649 in 2012, and 550 in 2013. The decline was primarily seen in blood cultures of nosocomial origin (Fig. 1). The incidence of nosocomial bacteremias due to *P. aeruginosa* steadily fell from a high of 0.148 episodes per 1000 bed days of care among the 107 facilities in 2007 to a low of 0.077 episodes per 1000 bed days of care in 2013 ($P < 0.05$), while the incidence of nonnosocomial bacteremias demonstrated no significant change.

Ciprofloxacin and/or levofloxacin were tested against 4671 specimens, representing the largest number of a single antibiotic (or pair of antibiotics) tested, followed by gentamicin with 4620 results reported,

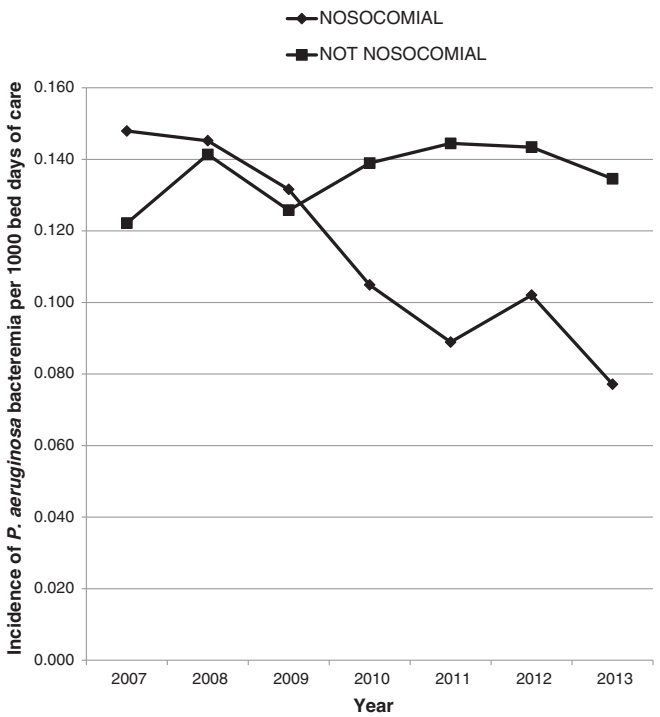

Fig. 1. Incidence per 1000 bed days of care of *P. aeruginosa* bloodstream isolates of nosocomial and nonnosocomial origins.