Diagnostic Microbiology and Infectious Disease 86 (2016) 460–463

Contents lists available at ScienceDirect

Diagnostic Microbiology and Infectious Disease

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

Solid organ transplant antibiograms: an opportunity for antimicrobial stewardship

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ARTICLE INFO

Article history:
Received 13 July 2016
Received in revised form 22 August 2016
Accepted 22 August 2016
Available online 26 August 2016

Keywords:
Antimicrobial susceptibility testing
Antibiogram
Transplantation

ABSTRACT

Objectives: We aimed to compare the antimicrobial susceptibility percentages in blood and urine bacterial isolates recovered from solid organ transplant (SOT) recipients with those reported in the hospital-wide antibiogram.
Methods: Retrospective review of the antimicrobial susceptibilities of bacterial isolates recovered from SOT recipients at a 1550-bed hospital over a 2-year period. Antibiograms were categorized by anatomic site (blood and urine). Percentage of bacterial susceptibilities to specific antibiotics were compared with the hospital-wide antibiogram.
Results: A total of 1889 unique cultures were identified. Blood and urine isolates of *Escherichia coli, Klebsiella pneumonia* and *Pseudomonas aeruginosa* had significantly lower susceptibility to first and second line antibiotics compared to the hospital-wide antibiogram.
Conclusion: Significant differences in susceptibilities between isolates from blood and urine cultures from SOT recipients and the hospital-wide antibiogram were found. A population-based strategy for the development of antibiograms specific for this group of high-risk patients could better guide appropriate empiric antimicrobial selection.

1. Introduction

Solid organ transplant (SOT) recipients are at an increased risk of infections with multi-drug resistant (MDRs) organisms due to multiple reasons, including immunosuppressive therapy, prolonged hospitalizations, and exposure to pre and post transplant antimicrobials for prophylaxis and treatment of infections (Green 2013). In patients suspected to have an infection, timely initiation of adequate empirical antimicrobial therapy has been associated with improved outcomes, including lower morbidity and mortality rates (Gaieski et al. 2010; Garnacho-Montero et al. 2003; Ibrahim et al. 2000). Inadequate empiric antimicrobial therapy is prescribed in more than half of SOT recipients hospitalized with infectious complications, resulting in approximately a 3.5-fold increase in mortality compared to patients who receive adequate empiric therapy (Hamandi et al. 2009).

Antibiograms are periodic summary reports of antimicrobial susceptibilities of local bacterial isolates submitted to the hospital's clinical microbiology laboratory. These reports are most valuable when used for selecting empiric antimicrobial therapy usually in emergency departments, critical care units and inpatient settings. The Clinical and Laboratory Standards Institute (CLSI) (2014) recommends that hospitals analyze and present a cumulative antimicrobial susceptibility report at least annually, using "only the first isolate of a species/patient/analysis period irrespective of body site or antimicrobial susceptibility profile". However, hospital-wide antibiograms may not reflect differences in susceptibility rates across the different units or specialized patient populations within a hospital (Binkley et al. 2006; Kuster et al. 2008; Namias et al. 2000). Furthermore, clinically relevant variations in susceptibility rates may exist between specimens from different anatomic sources (Kuster et al. 2008). These differences can potentially impact the efficacy of the antimicrobial regimens chosen in specific clinical scenarios (Namias et al. 2000).

We hypothesized that there are differences in the antimicrobial susceptibilities of the most frequent Gram-negative bacterial isolates from SOT recipients compared to our institution's hospital-wide antibiogram. Our primary endpoint was to compare the antimicrobial susceptibility percentages in blood and urine isolates of SOT recipients with those reported in the hospital antibiogram over a 2-year period.

2. Materials and methods

2.1. Setting

The study was conducted at Jackson Memorial Hospital, a 1558-licensed bed tertiary care teaching hospital in Miami, Florida. The

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http://dx.doi.org/10.1016/j.diagmicrobio.2016.08.018
0732-8893/

Miami Transplant Institute (MTI) is affiliated with Jackson Memorial Hospital and the University of Miami. Between 2013 and 2014, 980 SOT were performed at Jackson Memorial Hospital by the MTI, including adult and pediatric kidney (624), pancreas (25), combined kidney-pancreas (39), liver (231), heart (24), lung (4), and intestinal (33) (Organ Procurement and Transplantation Network 2016). SOT recipients are hospitalized in various units throughout the hospital depending on the transplanted organ and timing post transplantation. No outbreaks with MDR organisms occurred during the study period.

2.2. Susceptibility testing

All bacterial isolates were tested at the hospital's central microbiology laboratory. Antimicrobial susceptibility testing was performed using the Vitek 2 system (BioMériux®). Interpretative criteria for susceptibility and resistance were determined using the minimum inhibitory concentration breakpoint values established by the CLSI in 2010 (Clinical Laboratory Standards Institute 2010).

2.3. Hospital-wide antibiogram

The hospital-wide antibiogram was developed in accordance to CLSI criteria (Clinical Laboratory Standards Institute 2014). Antimicrobial susceptibility information was aggregated using WHONET®, a free Windows-based database software developed for the management and analysis of microbiology laboratory data with a special focus on the analysis of antimicrobial susceptibility test results (World Health Organization 2015). The hospital-wide antibiogram is reported every 6 months in the hospital's Antimicrobial Stewardship Program website. For the purposes of this study, antimicrobial susceptibility data from January 1, 2013 to December 31, 2014 was combined. This data included isolates belonging to SOT recipients. No individual patient information was collected.

2.4. Solid-organ transplant recipient antibiogram

The Infection Control and Antimicrobial Stewardship Surveillance System (Vigilanz®) was queried to obtain the results of all bacterial isolates from hospitalized patients flagged in the electronic medical record as SOT recipients during January 1, 2013 to December 31, 2014. Isolates were then categorized by anatomic site of recovery (e.g., blood, urine and other). For the purpose of this study, we focused on cultures from blood and urine only. Only the first isolate per patient and per anatomic site was included. Analysis was limited to the most prevalent organisms in order to meet epidemiological CLSI standards of minimum of 30 isolates per organism (Clinical Laboratory Standards Institute 2014). We included *Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa* since at our facility these are the most frequent Gram-negative bacteria recovered from SOT recipients.

2.5. Statistical methods

Antimicrobial susceptibility percentages for blood and urinary isolates of SOT recipients were compared with the hospital-wide aggregated percentages for the study period. Chi-square or Fisher's exact test were used as appropriate. A two-tailed *P* value of less than 0.05 was considered statistically significant. All analyses were performed using Stata 14 (College Station, TX).

3. Results

A total of 1889 unique cultures from SOT recipients were identified during the study period. Only the first isolate of each organism per patient and anatomical site were included: 606 (32%) isolates from urine, 399 (21%) from blood, and 884 (47%) from other anatomical sites. The hospital-wide antibiogram comprised results of 10,439 bacterial isolates, and included 5332 *E. coli* isolates, 2061 *K. pneumoniae* isolates, 1458 *P. aeruginosa* isolates, 1298 *E. faecalis* isolates, and 290 *E. faecium* isolates.

E. coli was the gram-negative organism most frequently isolated in urine cultures, present in 183 (30%), and in 43 (11%) of blood cultures of SOT recipients. Significantly lower percentages of susceptibility of *E. coli* to trimethroprim-sulfamethoxazole, levofloxacin, and ceftriaxone were seen in both blood and urine cultures of SOT recipients compared to the hospital wide antibiogram (Fig. 1).

K. pneumoniae was isolated from 139 (23%) urine cultures and 48 (12%) blood cultures of SOT recipients. Significant differences in susceptibility percentages of these organisms to all antibiotics tested were found both in urine and blood cultures from SOT recipients compared to the hospital-wide antibiogram, all with lower susceptibility rates than those seen in the hospital overall (Fig. 2). Amikacin was the only antimicrobial consistently active, with 92% of blood cultures isolates from SOT recipients susceptible to this agent, and 93% of urine isolates, however, this was still statistically significantly lower when compared to the 98% susceptibility rate observed in the hospital-wide antibiogram.

P. aeruginosa was isolated from 41 (7%) urine cultures and 16 (4%) blood cultures of SOT recipients. Among urine cultures of SOT recipients, the percentage of isolates susceptible to levofloxacin, cefepime, and amikacin was significantly lower compared to the hospital wide antibiogram (Fig. 3). Differences were also seen in susceptibility percentage of blood cultures of SOT recipients compared to the hospital-wide antibiogram, however there were only 16 isolates during the study period, which is below the minimum CLSI standards for statistical interpretation.

4. Discussion

Our results demonstrate that susceptibility rates for *E. coli, K. pneumoniae and P. aeruginosa* recovered from SOT recipients were significantly lower than those reflected in the hospital-wide antibiogram at our institution. Using data stratified by anatomic source, the percent of organisms resistant to first-line antimicrobials was greater among SOT recipients than would have been predicted by the hospital-wide antibiogram.

Different stratification strategies for the construction of cumulative antibiogram have been described but there is variation between studies and hospitals. Some authors have highlighted the value of unit-specific antibiograms since differences in susceptibility rates among units

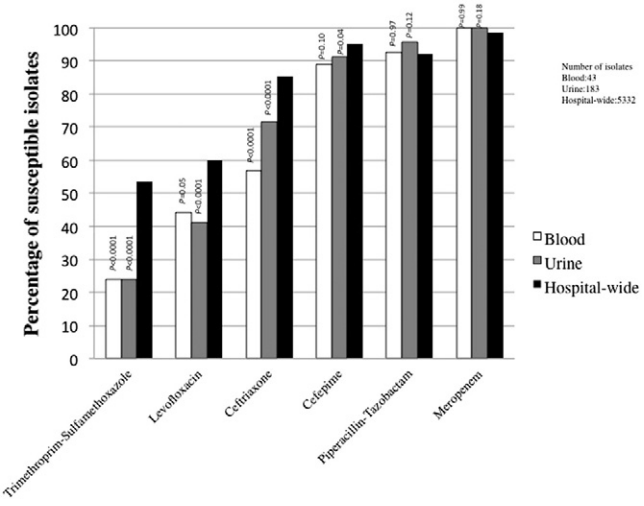

Fig. 1. Percentage of susceptible isolates of *Escherichia coli* from solid organ transplant recipient by anatomic source of culture compared to the hospital-wide antibiogram. *P*-values were determined by chi-square or Fisher's exact test and indicate comparisons between urine and blood cultures of solid organ transplant recipients and the hospital-wide antibiogram.