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Impact of inappropriate initial antibiotics in critically ill surgical patients with bacteremia

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Abstract

BACKGROUND: Bloodstream infections in critically ill patients are associated with mortality as high as 60% and a prolonged hospital stay. We evaluated the impact of inappropriate antibiotic therapy (IAAT) in a critically ill surgical cohort with bacteremia.

METHODS: This retrospective study evaluated adults with intensive care unit admission greater than 72 hours and bacteremia. Two groups were evaluated: appropriate antibiotic therapy (AAT) vs IAAT.

RESULTS: In 72 episodes of bacteremia, 57 (79%) AAT and 15 (21%) IAAT, mean age was 54 ± 17 years and APACHE II of 17 ± 8. Time to appropriate antibiotics was longer for IAAT (3 ± 5 IAAT vs 1 ± 1 AAT days, $P = .003$). IAAT was seen primarily with *Acinetobacter* spp (33% IAAT vs 9% AAT, $P = .01$) and *Enterococcus faecium* (26% IAAT vs 7% AAT, $P = .03$). If 2 or more bacteremic episodes occurred, *Acinetobacter* spp. was more likely, 32% vs 2%, $P = .001$.

CONCLUSIONS: AAT selection is imperative in critically patients with bacteremia to reduce the significant impact of inappropriate selection. Repeated episodes of bacteremia should receive special attention.

According to the Centers for Disease Control and Prevention, 1.7 million healthcare-associated infections occur each year in the United States.[1] When these infections occur in the intensive care unit (ICU) population, morbidity, mortality, and length of stay (LOS) are greatly increased.

Antimicrobial-resistant pathogens pose an enormous and increasing challenge to clinicians. It is known that inappropriate antibiotic therapy (IAAT) for bacteremias can increase mortality by up to 60%.[2,3] Patients diagnosed with a bacteremia should be treated quickly and appropriately to minimize the negative sequelae. We evaluated the effects of inappropriate initial empiric antibiotics in our intensive care surgical patients to determine the impact on mortality and LOS.

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The authors declare no conflicts of interest.

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Methods

This Institutional Review Board approved retrospective cohort study evaluated patients admitted to the surgical ICU for over 3 and a half consecutive years from January 2006 to June 2009. Criteria for inclusion were age $\geq$ 18 years, admission to the ICU for greater than 72 hours, and development of one or more episodes of bacteremia. Patients were identified from health information management, epidemiology, and microbiology laboratory department records.

In accordance with the Center of Disease Control's National Healthcare Safety Network, bloodstream infections were defined as either a recognized pathogen cultured from one or more blood cultures or common skin flora cultured from 2 or more blood cultures within 2 hours of each other.[4] Although the definition of catheter-related blood stream infections was changed by the Centers of Medicare and Medicaid in 2009, we chose to maintain the prior definition based on clinical bedside practice.

Blood cultures were obtained primarily by nursing personnel and sent to the laboratory for analysis. Blood cultures were obtained based on a set protocol: 2 sets collected 15 minutes apart with each set containing 1 aerobic bottle and 1 anaerobic bottle, 10 mL of blood per bottle. Our Department of Microbiology used MicroScan in the identification of organisms and determination of susceptibilities.

The initial empiric antibiotic therapy was deemed appropriate if: (1) the initial antibiotics were administered within 24 hours after the blood cultures were obtained; (2) the organism was susceptible to at least one of the antibiotics or antifungals administered; and (3) dosing and route of administration met standard drug recommendations.[5]

The time to initial appropriate antibiotic therapy (AAT) was defined as the time from the initial positive culture was reported by microbiology until appropriate antibiotics were administered. Repeat episodes of bacteremia were identified if the original pathogen had resolved as proven by a negative repeat blood culture, and the same or different pathogen was isolated at a separate time period. The time of day the culture was reported positive was evaluated to determine if a difference existed. Patients were divided into 2 groups: AAT and inappropriate antibiotic therapy (IAAT).

All statistical analyses were performed using SPSS version 21.0 and are primarily descriptive. Data are expressed in mean $\pm$ standard deviation. Students' *t*-test was used to compare continuous variables, and Pearson's chi-square test was used to compare categorical variables.

Results

During the 3 and half years of the study, 382 patients were admitted to the surgical ICU and evaluated. Of these, 55 (14%) patients had 72 separate episodes of bacteremia based on our definitions. This infection rate was 6.2 per 1,000 patient days. The patients were 54 $\pm$ 17 years of age, 65% male, 73% African American, with a mean APACHE II score 17 $\pm$ 8. The demographic and clinical characteristics were not different between AAT and IAAT (Table 1). The top 3 isolates identified were *Staphyloccoccus coagulase* negative (20%), *Enterococcus* spp. (20%), and *Acinetobacter baumannii* (11%; Table 2). The primary source of bacteremia was a venous catheter with patients having a triple lumen central venous catheter (CVC) 82% of the time, a peripherally inserted central catheter (PICC) 27% of the time, and concomitant PICC and CVC 20% of the time. The coinfections present included pneumonia (16%) and urinary tract infections (13%).

For the 72 episodes of bacteremia, 57 (79%) received AAT and 15 (21%) received IAAT. The most common empiric antibiotic regimen was cefepime (32%) and weight-based dosing of vancomycin (58%) to cover for the typical nosocomial pathogens such as *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*, respectively.

Time to initial appropriate antibiotics was longer for IAAT vs AAT, (2 $\pm$ 4 vs 1 $\pm$ 1 day, $P = .003$). IAAT was seen primarily with *Acinetobacter* spp (33% IAAT vs 9% AAT, $P = .01$) and *Enterococcus faecium* (26% IAAT vs 7% AAT, $P = .03$) isolates.

Repeated episodes of bacteremia occurred 39% of the time overall, 35% AAT vs 53% IAAT, $P = .19$. *Acinetobacter* spp. was more likely to be isolated on the 2nd episode, 32% $\geq$ 2 episodes vs 2% 1 episode of bacteremia, $P = .001$. If 2 or more episodes of bacteremia occurred, surviving patients had a prolonged hospital LOS (99 $\pm$ 67 vs 42 $\pm$ 32 days, $P = .001$), ICU LOS (84 $\pm$ 63 vs 31 $\pm$ 27 days, $P < .001$), and longer duration of mechanical ventilation (78 $\pm$ 70 vs 21 $\pm$ 24 days, $P < .001$).

In surviving patients (n = 44), hospital LOS was longer with IAAT, (83 $\pm$ 53 vs 47 $\pm$ 43 days, $P = .04$). ICU LOS was longer but not significant with IAAT (58 $\pm$ 51 vs 38 $\pm$ 40 days, $P = .19$).

Overall, no difference was seen in-hospital mortality rates, 19% AAT vs 25% IAAT, $P = .68$. However, death was more likely when IAAT was prescribed during the night (7 PM to 7 AM) vs AAT, (27% vs 4%, $P = .02$). Time to AAT in patients who had antibiotics initiated during the night was not different, .3 $\pm$ .5 vs 3.8 $\pm$ 8.2 days, $P = .19$.

Evaluating mortality based on the specific pathogens, patients with inappropriate initial antibiotic therapy were more likely to die (80% vs 22%, $P = .02$). In-hospital mortality was significantly higher when the following variables were also present: lactic acidosis (lactate >4 mmol/L), $P < .001$, age $\geq$ 50 years, $P = .01$, and when *Acinetobacter* spp. was found on culture, $P = .02$.

Risk factors for bacteremia were not significant on univariate analysis. Risk factors evaluated included urethral foley catheter, CVC or PICC, surgical procedure, mechanical ventilation, severe hypoalbuminemia (serum albumin <2gm/dL), or administration of parenteral nutrition.