080. Improving Definitive Therapy Among Patients with Methicillin-resistant Staphylococcus aureus Bloodstream Infections: Predictors of Early Therapeutic Switch to Linezolid or Daptomycin

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Session: 76. Treatment of Resistant Infections - Clinical Analyses Thursday, October 5, 2017: 12:30 PM

Background. Vancomycin is a first-line antibiotic for treating methicillin-resistant St. aureus bloodstream infections (MRSA BSI), due to its activity against MRSA and low cost. If vancomycin fails, patients are often switched to daptomycin or linezolid. We aimed to determine predictors for switching from vancomycin to daptomycin or linezolid. Close follow-up and early identification of patients who may benefit from these newer antibiotics could improve outcomes.

Methods. Retrospective cohort study of all Veteran patients with MRSA BSI who began therapy on vancomycin from 2007 to 2014. Patients were followed for 30 days. Potential predictors of switching measured at the time of admission included demographic, diagnoses, and comorbidities. Co-infections were identified using ICD-9 codes. Additional predictors were time-varying during index admission, including: therapeutic level of vancomycin (defined as 24-hour area under concentration-time-curve to minimum inhibitory concentration ratio [MIC]) for 48 hours, 9.19% of DNP or 10.5% (n = 1,873) to linezolid. 4,763 (27%) patients had a therapeutic vancomycin level within 5 days of initiating vancomycin; 1,318 (7%) had a subtherapeutic level, and 11,760 (66%) could not have an AUC calculated. 5,692 (31.9%) patients experienced AKI after initiating vancomycin. Factors associated with increased likelihood of switching included subtherapeutic vancomycin dose [hazard ratio (HR) = 1.53; 95% confidence interval (CI): 1.29, 1.82]; AKI (HR = 1.51; 95% CI: 1.35, 1.67); coinfections with osteomyelitis (HR = 1.28; 95% CI: 1.13, 1.46); pneumonia (HR = 1.35; 95% CI: 1.10, 1.66) and endovascular infections (HR = 1.18; 95% CI: 1.05, 1.32).

Conclusion. A high proportion of patients with MRSA bacteremia were therapeutically managed. Close follow-up and co-infections may be targets for early data-driven daptomycin or linezolid therapy. Efforts should continue towards improving vancomycin dosing during the first 5 days of therapy.

Disclosures. M. Schweizer, B Braun: Speaker at a course, Travel reimbursement to attend course.

801. The Clinical Impact of Daptomycin Non-susceptible Enterococcus Bacteremia in Hematologic Malignancy

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Session: 76. Treatment of Resistant Infections - Clinical Analyses Thursday, October 5, 2017: 12:30 PM

Background. Patients with hematologic malignancies are prone to colonization and infection with vancomycin-resistant Enterococcus (VRE), and VRE bloodstream infections (BSI) in this population have been associated with a 30-day all-cause mortality of 40%. Daptomycin non-susceptible Enterococcus/DNSE are on the rise, with institutional rates as high as 15%. The objective of this study was to determine the attributable mortality associated with resistance to daptomycin among VRE isolates.

Methods. We performed a retrospective cohort study of hematologic malignancy patients who developed either DNSE or daptomycin-susceptible VRE bacteremia at the University of Alabama from January 1, 2008 and December 31, 2016. Categorical variables were analyzed using the Chi-square test or Fisher’s exact test when appropriate. A p-value <0.05 was considered significant.

Results. 34 patients were evaluated with 164 meeting the inclusion criteria. Seventy-three patients in the capped group vs. 91 in the non-capped group. Most common infections included ABSSSI, pneumonia and bacteremia. Mean weight 110 kg in capped vs. 108 kg in non-capped, mean age 52 ± 58, male 63% vs. 70%, fever resolution 83% vs. 60%, CMI 3.19 vs. 3.43 Six patients (8.2%) in the capped group were readmitted with bloodstream infections compared with 6 (6.6%) in the non-capped group, respectively. Six (9.6%) patients in the capped group experienced nephrotoxicity compared with 21 (23.1%) in the non-capped group (P = 0.04).

Conclusion. The capped group experienced lower mortality compared with the non-capped group (P = 0.001). When doses were capped, approximately $1,400 was saved per patient.

Disclosures. All authors: No reported disclosures.

802. Evaluation of telavancin dose capping in a large community hospital

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Session: 76. Treatment of Resistant Infections - Clinical Analyses Thursday, October 5, 2017: 12:30 PM

Background. Telavancin is a bactericidal lipoglycopeptide treat susceptible Gram-positive pathogens including Methicillin-resistant Staphylococcus aureus. Pharmacokinetic studies have shown that obese patients have increased exposure to telavancin compared with non-obese patients. Dose capping of 750 mg was utilized in selected patients with the purpose of minimizing toxicity and decreasing costs without compromising efficacy.

Methods. Retrospective case series includes adult patients admitted from 2010–2016 who received at least three doses of telavancin. Data collection includes patient demographics, telavancin dosing, antibiotic indication, length of stay, laboratory and microbiological data, and risk index (CMI). The primary outcome is to assess the efficacy of capping telavancin doses at 750 mg compared with non-capped doses. Secondary outcomes include safety and financial outcomes, as well as readmission rates.

Results. 333 patients were evaluated with 164 meeting the inclusion criteria. Seventy-three patients in the capped group vs. 91 in the non-capped group. Most common infections included ABSSSI, pneumonia and bacteremia. Mean weight 110 kg in capped vs. 108 kg in non-capped, mean age 52 ± 58, male 63% vs. 70%, fever resolution 83% vs. 60%, CMI 3.19 vs. 3.43 Six patients (8.2%) in the capped group were readmitted with bloodstream infections compared with 6 (6.6%) in the non-capped group, respectively. Six (9.6%) patients in the capped group experienced nephrotoxicity compared with 21 (23.1%) in the non-capped group (P = 0.04).

Conclusion. The use of a capped 750 mg telavancin dose in adult patients appears to be an alternative dosing scheme that maintains efficacy and safety as well as being associated with reduced cost. Additional clinical and pharmacokinetic and clinical studies are needed to further investigate the use of capped dosing of telavancin to support the findings of this retrospective case series.

Disclosures. All authors: No reported disclosures.

803. Impact of minocycline, polymyxin B, meropenem, and amikacin on growth-prevention of Acinetobacter baumannii with various biofilm-forming capabilities

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Session: 77. Use of PK/PD to optimize existing antibiotics and antifungals Thursday, October 5, 2017: 12:30 PM

Background. Acinetobacter baumannii is a clinically challenging pathogen with biofilm (BF) forming capabilities, making eradication difficult. The objective of this study was to compare in vitro activity of minocycline, polymyxin B, meropenem, and amikacin and evaluate the effectiveness in preventing BF formation utilizing previously validated methodology.

Methods. Minimum inhibitory concentrations (MIC) were performed on all isolates in duplicate using CLSI standards. Tryptic soy broth plus 1% dextrose (TSB-D1%) was used to quantify BF formation of 12 clinically unique and diverse strains of A. baumannii. Biofilm formation and concentration (BF) was defined as follows: the concentration of drug where no biofilm attachment was observed, as determined by optical density (OD). BPC was determined by evaluating increasing concentrations of antibiotic in TSB-D1% for 48 hours. BF was quantified by measuring OD of each well at 570nm via spectrophotometer. Previously described BF adherence categories were utilized to define BF strength (OD570 > 2 = strong; OD570 1–2 = moderate; OD570 <0.5 < 1 = weak; OD570 ≤ 0.5 = none).

Results. Twelve clinical isolates were evaluated with a full range of BF formation capabilities. Prevention of BF formation was observed at concentrations below the MIC by 2.57-4.12-fold for minocycline, 5.57-8.97-fold for polymyxin B, 5.77 to 17.56-fold for meropenem, and 0.72 to 0.35-fold for amikacin. Minocycline prevented BF formation at or below the MIC for 75% of isolates tested vs. 67% for polymyxin B, 33% for meropenem, and 33% for amikacin. Free drug concentrations at the end of a dosing interval, derived from pharmacokinetic data, imply that BF would be prevented for 75% of minocycline-exposed isolates vs. 58.3% polymyxin B, 8.3% meropenem, and 8.3% amikacin-exposed isolates.

Conclusion. Minocycline, polymyxin B and meropenem prevented BF formation at clinically relevant concentrations. Prompt antibiotic administration may...