800. 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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Background. Vancomycin is a first-line antibiotic for treating methicillin-resistant *S. 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 demographics, diagnoses, and comorbidities. Co-infections were defined 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 [AUC/MIC] ≥ 400), lab values, and acute kidney injury (AKI, defined by change in creatinine). A Cox proportional hazards model was used to evaluate the association between predictors and the relative hazards of switching to daptomycin or linezolid.

Results. 17,841 patients had MRSA BSI and were given vancomycin initially. By 30 days, 18% of patients were therapeutically switched including 9.4% (n = 1,680) to daptomycin and 10.5% (n = 1,873) to linezolid. 4,763 (27%) patients had a therapeutic vancomycin dose within 5 days of initiating vancomycin, 1,318 (7%) had a subtherapeutic dose, 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: 1.34, 1.70); co-infections 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 switched. Patients with co-infections may be targets for early daptomycin/linezolid therapy. Efforts should continue towards improving vancomycin dosing during the first 5 days of therapy.

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

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Background. Patients with hematologic malignancies are prone to colonization and infection with vancomycin-resistant E*nterococcus* (VRE), and VRE blood stream infections (BSI) in this population have been associated with a 30-day all-cause mortality approaching 40%. Daptomycin nonsusceptible *Enterococci*(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 between January 1, 2008 and December 31, 2016. Categorical variables were analyzed with chi-square or Fisher's exact test and continuous variables were analyzed with a t-test or Wilcoxon rank sums test when appropriate. A p-value <0.05 was considered significant.

Results. 34 cases of DNSE and 65 cases of VRE were identified. There were no significant differences noted in demographic data. At time of bacteremia, both DNSE and VRE cohorts had similar APACHE II scores (medians for DNSE and VRE were 19). The DNSE cohort had longer periods of neutropenia prior to the diagnosis of bacteremia [median 32.1 days vs.. 19.3 days, OR 1.85 95% CI (0.75-1.60)]. Patients with DNSE had a longer time to initiation of appropriate antibiotics (median 3.5 days vs. 2.0 days, P = 0.01). There were similar rates of bone marrow transplantation (53 % of DNSE vs. 51% of VRE), however, DNSE cases were more likely to develop graft vs. host disease [OR 3.6 95% CI (1.07-12.38)]. In the 90-day period prior to bacteremia, daptomycin exposure occurred in only 12 (35.3%) of DNSE cases vs.. 1 (1.5%) VRE case [OR 34.9 95% CI (4.3-284.1)]. Median lengths of stay (LOS) were similarly high in both groups, however, DNSE patients were more likely to have a LOS over 50 days as compared with VRE (P = 0.048). 30-day mortality in the DNSE cohort was 50% compared with 38% in the VRE group (P = 0.12).

Conclusion. In a retrospective study, the 30-day mortality associated with DNSE bacteremia was 50%. Infection prevention interventions targeting this particular multi-drug-resistant organism are warranted in this vulnerable population.

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

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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 case mix 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 ABSSI, pneumonia and bacteremia. Mean weight 110 kg in capped vs. 108 kg in noncapped, mean age 52 vs. 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 and 6 (8.5%) needed additional antibiotics compared with 12 (13.2%) and 9 (9.9%) in the non-capped group, respectively. Seven (9.6%) patients in the capped group experienced nephrotoxicity compared with 21 (23.1%) in the non-capped group (P = 0.04). The capped group experienced 7 (9.6%) incidents of mortality vs. 28 (30.8%) in the non-capped group (P = 0.001). When doses were capped, approximately $1,400 was saved per patient.

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 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.

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

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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 prevention concentration (BPC) was defined as 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 (OD_{570} > 2 = strong; OD_{570} 1–2 = moderate; OD_{570} >0.5 <1 = weak; $OD_{570} \leq 0.5$ = 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 ± 17.56-fold for meropenem, and 0.72 ± 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 antimicrobial administration may