

Disclosures. All Authors: No reported Disclosures.

1955. Novel Compound Reverses Vancomycin Resistance in Vancomycin-resistant Enterococci (VRE)

Kenneth Onyedibe, MBBS, MSc, FWACP, FMCPath¹; Neetu Dayal, PhD² and Herman Sintim, PhD²; ¹Purdue Institute for Immunology, Inflammation and Infectious Diseases, Purdue University, West Lafayette, Indiana; ²Purdue Institute for Drug Discovery, Purdue University, West Lafayette, Indiana

Session: 227. Novel Antimicrobials and Approaches Against MDR Organisms
Saturday, October 5, 2019: 11:30 AM

Background. *Enterococcus* causes 14% of all hospital-associated infections (HAIs) according to Centers for Disease Control and Prevention (CDC) data. 35.5% of these HAIs are caused by Vancomycin-resistant *Enterococci* (VRE) including highly fatal bacteremia, surgical site infections, and urinary tract infections. We present a novel synthetic compound, HSD 03-21 that could make VRE completely susceptible to vancomycin in-vitro.

Methods. HSD 03-21 was synthesized de novo from a hydroxybenzylidene – indolinone backbone in our laboratory. The minimum inhibitory concentration (MIC) of HSD 03-21 and vancomycin against VRE were determined according to clinical laboratory standards institute (CLSI) guidelines. The standard checkerboard assay was used to determine vancomycin-HSD 03-21 interactions against VRE. Briefly, HSD 03-21 and vancomycin at 10 mg/mL were prepared and diluted serially along the ordinate and abscissa of 96-well microtiter plates, respectively. Bacteria was standardized using the 0.5 McFarland standard, diluted (1:100), aliquoted into respective wells and incubated at 37°C for 18–20 hours. All assays were run in triplicates. The fractional inhibitory concentration (FIC) index was calculated for each combination. The FIC of either agent was calculated as: FIC (vancomycin) = MIC of vancomycin in combination/MIC of vancomycin alone and FIC (HSD 03-21) = MIC of HSD 03-21 in combination/MIC of HSD 03-21 alone. The cumulative FIC index Σ FICI was then calculated as: Σ FIC = FIC(vancomycin) + FIC(HSD 03-21). The calculated Σ FIC indices were interpreted as synergistic if Σ FIC: ≤ 0.5 .

Results. The MIC of vancomycin for VRE faecalis was 256 $\mu\text{g mL}^{-1}$ while that of HSD 03-21 was 128 $\mu\text{g mL}^{-1}$. When vancomycin was combined with HSD 03-21 at 8 $\mu\text{g mL}^{-1}$ (1/16 MIC), there was a reduction in MIC of vancomycin to 0.5 $\mu\text{g mL}^{-1}$. The combination showed excellent synergy with Σ FIC of 0.06.

Conclusion. HSD 03-21 reduced the MIC of vancomycin from 256 to 0.5 $\mu\text{g mL}^{-1}$. This has an immense potential of changing the way we use vancomycin and in the treatment of VRE infections. Translation of this novel compound could save thousands of lives from VRE and the failures and inherent toxicities of current doses of vancomycin.

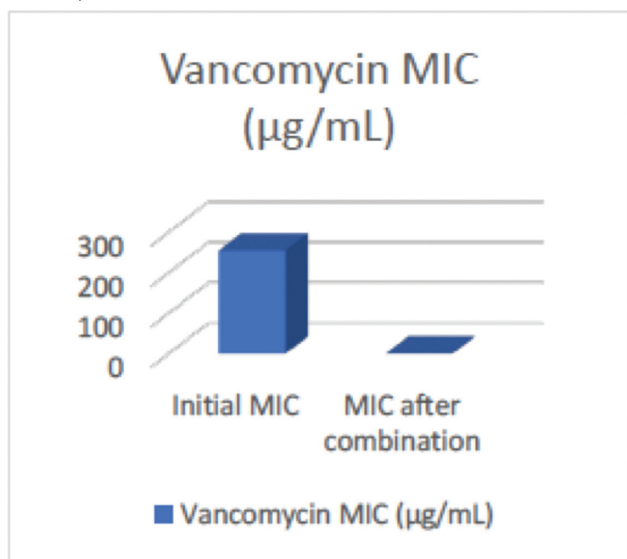


Figure 1. 500 fold reduction in vancomycin MIC

Disclosures. All Authors: No reported Disclosures.

1956. Reduction in Endotracheal Aspirate Cultures after Implementation of a Diagnostic Stewardship Intervention in a Pediatric Intensive Care Unit

Anna Sick-Samuels, MD, MPH¹; Jules Bergmann, MD¹; Matthew Linz, BS¹; James Fackler, MD¹; Sean Berenholtz, MD¹; Joe Dwyer, MAEd, EdD(c), RRT²; Katherine Hoops, MD, MPH¹; Elizabeth Colantuoni, PhD³ and Aaron Milstone, MD, MHS¹; ¹Johns Hopkins University School of Medicine, Baltimore, Maryland; ²Johns Hopkins Hospital, Baltimore, Maryland; ³Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

Session: 228. Pediatric Stewardship
Saturday, October 5, 2019: 10:30 AM

Background. Clinicians obtain endotracheal aspirate (ETA) cultures from mechanically ventilated patients in the pediatric intensive care unit (PICU) for the evaluation of ventilator-associated infection (i.e., tracheitis or pneumonia). Positive cultures prompt clinicians to treat with antibiotics even though ETA cultures cannot distinguish bacterial colonization from infection. We undertook a quality improvement initiative to standardize the use of endotracheal cultures in the evaluation of ventilator-associated infections among hospitalized children.

Methods. A multidisciplinary team developed a clinical decision support algorithm to guide when to obtain ETA cultures from patients admitted to the PICU and ventilated for >1 day. We disseminated the algorithm to all bedside providers in the PICU in April 2018 and compared the rate of cultures one year before and after the intervention using Poisson regression and a quasi-experimental interrupted time-series models. Charge savings were estimated based on \$220 average charge for one ETA culture.

Results. In the pre-intervention period, there was an average of 46 ETA cultures per month, a total of 557 cultures over 5,092 ventilator-days; after introduction of the algorithm, there were 19 cultures obtained per month, a total of 231 cultures over 3,554 ventilator-days (incident rate 10.9 vs. 6.5 per 100 ventilator-days, Figure 1). There was a 43% decrease in the monthly rate of cultures (IRR 0.57, 95% CI 0.50–0.67, $P < 0.001$). The ITSA revealed a pre-existing 2% decline in the monthly culture rate (IRR 0.98, 95% CI 0.97–1.00, $P = 0.01$), an immediate 44% drop (IRR 0.56, 95% CI 0.45–0.69, $P = 0.02$) and a stable rate in the post-intervention period (IRR 1.03, 95% CI 0.99–1.07, $P = 0.09$). The intervention led to an estimated \$6000 in monthly charge savings.

Conclusion. Introduction of a clinical decision support algorithm to standardize the obtaining of ETA cultures from ventilated children was associated with a significant decline in the rate of ETA cultures. Additional investigation will assess the impact on balancing measures and secondary outcomes including mortality, duration of ventilation, duration of admission, readmissions, and antibiotic prescribing.

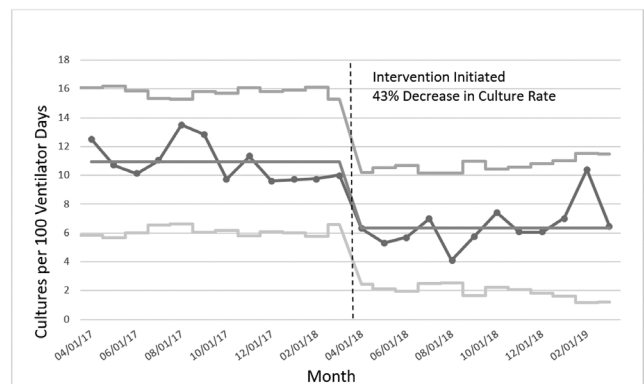


Figure 1. Monthly rate of endotracheal aspirate cultures per 100 ventilator-days in the pediatric intensive care unit. This control chart shows the monthly rate, upper and lower limits, and the overall rate before and after introduction of the intervention in April 2018.

Disclosures. All Authors: No reported Disclosures.

1957. Impact of β -Lactam Antibiotic Allergy on Antimicrobial Use, Clinical Outcomes, and Costs for Hospitalized Children

Trahern Wallace Jones, MD¹; Nora Fino, MS¹; Jared Olson, PharmD¹; Lauri Hicks, DO²; Katherine E. Fleming-Dutra, MD² and Adam Hersh, MD, PhD³; ¹University of Utah School of Medicine, Salt Lake City, Utah; ²Centers for Disease Control and Prevention, Atlanta, Georgia; ³University of Utah, Salt Lake City, Utah

Session: 228. Pediatric Stewardship
Saturday, October 5, 2019: 10:45 AM

Background. Most β -lactam antibiotic allergies (BLA) are incorrectly diagnosed and could be de-labeled. Adult patients with BLA are more likely to receive broader-spectrum antimicrobials and experience worse health outcomes than nonallergic patients. Similar studies on the impact of BLA on antimicrobial use and clinical outcomes are limited in pediatrics. Our objective was to compare antimicrobial use, and clinical and economic outcomes between hospitalized children with and without BLA.

Methods. This was a retrospective cohort of pediatric patients hospitalized at an Intermountain Healthcare (IH) hospital from 2007 to 2017. IH has 22 hospitals including one children's hospital. Patients aged 30 days-17 years who received ≥ 1 dose of an antimicrobial during hospitalization were included. The exposure variable was the presence of BLA (penicillins or cephalosporins) in the allergy field of the medical record. Patients with BLA were matched to nonallergic controls on age, sex, race, clinical service line, admission date, children's hospital or other hospital, and co-morbid conditions. We used multivariable log-transformed-linear and logistic regression models to compare patients with BLA to controls in terms of antibiotic selection and total antimicrobial days, antimicrobial cost, length-of-stay (LOS) and 30-day readmission. For antibiotic selection we examined the odds of receiving the following broader-spectrum agents individually and in composite: vancomycin, fluoroquinolones, clindamycin, carbapenems, and macrolides.