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Session: O-27. Innovation in Antimicrobial Stewardship

Background: Concomitant vancomycin and piperacillin-tazobactam use (CVPTU) for >2 days is associated with increased nephrotoxicity. At Vanderbilt University Medical Center, a sustained decline in CVPTU was achieved. A retrospective review of CVPTU and antimicrobial stewardship (AS) interventions was performed to develop a model for future AS quality improvement (QI) initiatives.

Methods: Data for adults receiving CVPTU January 2015 - August 2019 were extracted. No patients were excluded. Change in monthly incidence of CVPTU >2 days in relation to AS interventions was the primary outcome. CVPTU was analyzed with statistical process control (SPC) charts (QI Macros 2019). AS interventions were amassed from AS emails, meeting minutes, presentations and patient-specific interventions. We created a new intervention evaluation tool using the Hierarchy of Effectiveness (1-Education, 2-Policy, 3-Reminders, 4-Simplification, 5-Automation, 6-Forced Function) and a self-designed scale of impact (1-divisional subgroup, 2-division, 3-department, 4-center-wide). Scores were summed for each 6-month period and rated as low, moderate or high intervention strength. Periods were mapped against their corresponding CVPTU rate (Figure 1).

Results: *CVPTU Data*: During periods 1–5 (January 2015 - February 2018), an average 4% of admitted patients received >2 days CVPTU, decreasing to < 1% from period 5 (March 2018) onward (Figure 1). From period 1–5, an average 52.8% of patients with CVPTU received >2 days and dropped to 41.3% from period 5 onward (Figure 2).

Intervention Data: There was 1 low, 3 moderate and 4 high intensity periods. Intensity decreased as initiatives transitioned from behavior change to sustained behavior (Figure 1). The main interventions were education and patient-specific feedback. Division-specific antibiotic algorithms and computerized order sets re-enforced behavior. Infectious diseases consults and team pharmacists embedded the concept in daily practice.

Figure 1: Proportion of All Admissions with Concomitant Vancomycin and Piperacillin-Tazobactam Use (CVPTU) for >2 Days Mapped Against Simultaneous Quality Improvement Interventions.

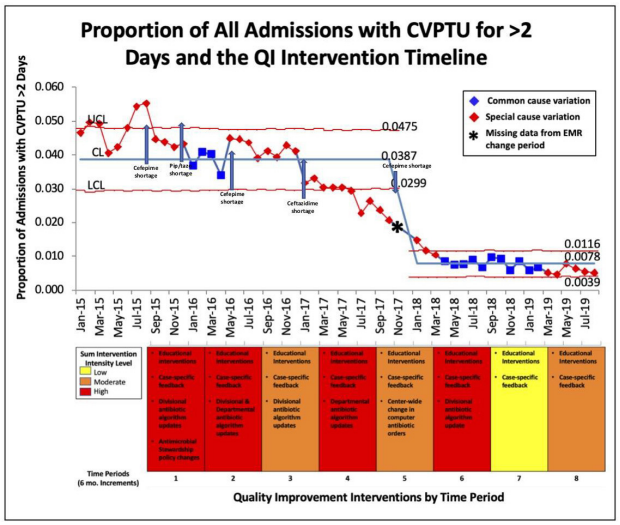
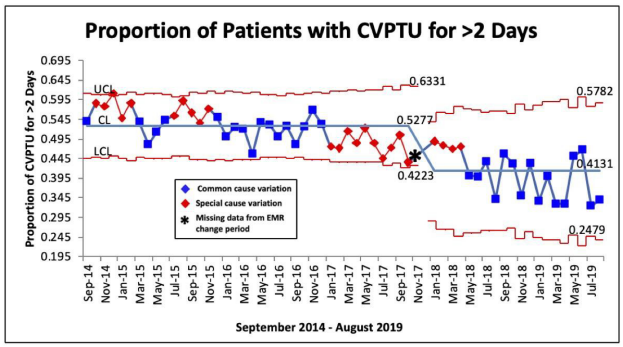


Figure 2: Proportion of Patients with Concomitant Vancomycin and Piperacillin-Tazobactam Use (CVPTU) for >2 Days.



Conclusion: Persistent, repetitive center-wide intervention is key to driving and sustaining change. More analysis of specific intervention types and impact of external factors would enhance understanding and future use of this AS change implementation model.

Disclosures: **All Authors**: No reported disclosures

142. Frequency of Short-course Empiric Antibiotic Use as an Antimicrobial Stewardship Metric

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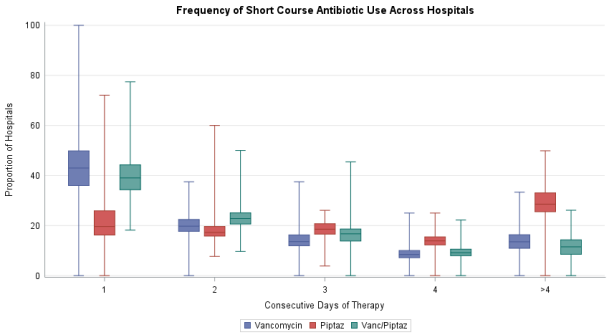
Session: O-27. Innovation in Antimicrobial Stewardship

Background: Antimicrobial stewardship metrics that provide actionable guidance are needed to support efforts to improve hospital use of antibiotics. Antibiotics such as vancomycin and piperacillin/tazobactam are common empiric agents used frequently when the infectious process remains unknown. Thus short, incomplete courses of therapy are used more frequently for such agents. We aimed to evaluate the variability in short courses of vancomycin and piperacillin/tazobactam use across U.S. hospitals.



Methods: We performed a cross-sectional study among U.S. hospitals that contributed inpatient pharmacy data to the Vizient clinical database in 2016. We identified vancomycin and piperacillin-tazobactam courses initiated within the 48 hours of admission, measured as days of therapy received. We calculated the percent of patients that received 1, 2, 3, 4 or >4 days of therapy at each facility to describe short course empiric therapy use. To describe the variability across facilities, we then assessed the median, interquartile range (IQR), and total range of that percentage.

Results: We identified 145 hospitals representing approximately 3.7 million patient encounters for inclusion in this study. Within 48 hours of admission, 13.9% of encounters received vancomycin, 7.7% piperacillin/tazobactam, and 4.6% received both. The figure demonstrates the variability in the frequency of short course antibiotic use across hospitals; boxes indicate the IQR with the transecting line representing the median and whiskers representing the full range. The proportion of patients that received one day of therapy varied most across hospitals, with vancomycin ranging from 0–100%. In contrast, the frequency of patients that received greater than four days of therapy varied considerably less across hospitals; 0–33% for vancomycin.

Conclusion: The variability in use of short course empiric therapies suggests that use for non-infectious processes or infections not appropriately treated by these agents varies greatly across facilities. Measuring short course use for common empiric agents may serve as an important antimicrobial stewardship metric. Such a metric could inform antimicrobial stewardship efforts to reduce unnecessary initiation of empiric antimicrobial therapy.

Disclosures: **All Authors**: No reported disclosures

143. Modification of Linezolid Restriction Criteria Reduces ICU Gram-positive Antibiotic Consumption

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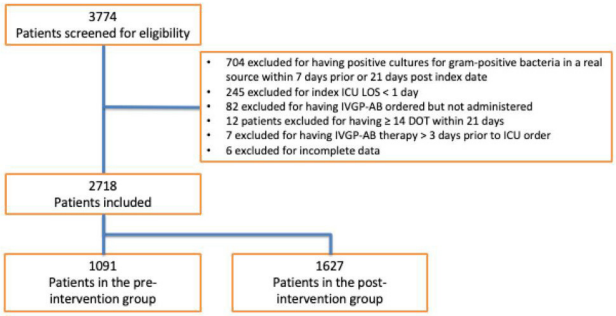
Session: O-27. Innovation in Antimicrobial Stewardship

Background: Antibiotic time out (ATO) policies have been proposed by the Centers for Disease Control and Prevention to limit unnecessary use of antibiotics. Critically ill patients are often treated empirically with MRSA-active agents for a prolonged duration. The objective of this study was to assess the impact of an ATO policy by targeting empiric gram-positive coverage.

Methods: Before this intervention, linezolid required pre-approval by the antimicrobial stewardship program or infectious diseases (ID) consult service before dispensing, and no automatic ATO policy was in place for any agent. In 2018, restriction of linezolid was modified to allow 72 hours of empiric use in the intensive care unit

(ICU). This retrospective, single-center, pre- post-intervention study looked at eight ICUs at our institution from two equal periods. Adults (age ≥ 18 years) were included who received an IV gram-positive antibiotic (IVGP-AB), specifically linezolid or vancomycin, used for empiric therapy and were admitted to the ICU. The primary outcome was antimicrobial consumption of IVGP-AB defined as days of therapy (DOT) per patient. Secondary outcomes included in-hospital length of stay (LOS), ICU LOS, in-hospital mortality, 30-day readmission, and incidence of acute kidney injury (AKI).

Figure 1. Flowchart of patient inclusion into the study



Results: 2718 patients met criteria for inclusion in the study. 1091 patients were included in the pre-intervention group and 1627 patients were included in the post-intervention group. Baseline characteristics between the two groups were similar, with ID consults being higher in the pre-intervention group. Total mean DOT of IVGP-AB in pre- and- post-intervention groups was 4.97 days vs. 4.36 days, p< 0.01. Secondary outcomes of in-hospital LOS, ICU LOS, and in-hospital mortality did not vary significantly between groups. Thirty-day readmission was lower in the post-intervention group (12.9% vs. 3.9%, p< 0.01). AKI did not differ significantly between groups, however the need for renal replacement therapy was higher in the pre-intervention group (1.2% vs. 0.2%, p< 0.01).

Table 1. Baseline Characteristics of Study Participants

Characteristic	Pre-Intervention Group (N=1091)	Post-Intervention Group (N=1627)	P Value
Age – Mean (SD), years	58.6 (± 16.2)	59.4 (± 16.2)	0.23
Male sex – no. (%)	668 (61.2)	956 (58.8)	0.20
White race – no. (%)	806 (73.9)	1182 (72.7)	0.51
ID Consult – no. (%)	385 (35.3)	513 (31.5)	0.04
Time from ICU admission to antibiotic order - Median (IQR), days	0.731 (2.75)	0.523 (2.18)	0.20
Ventilator- no. (%)	347 (31.8)	571 (35.1)	0.08

Abbreviations: ID, infectious diseases; ICU, intensive care unit

Table 2. Primary and Secondary Outcomes

Outcome	Pre-Intervention Group (N=1091)	Post-Intervention Group (N=1627)	P Value
Total DOT IVGP-AB- Mean (SD), days	4.97 (± 4.31)	4.36 (± 3.38)	<0.01
DOT Vancomycin- Mean (SD), days	4.93 (± 4.31)	3.87 (± 3.39)	<0.01
DOT Linezolid- Mean (SD), days	0.05 (± 0.55)	0.49 (± 1.51)	<0.01
In-hospital LOS- Mean (SD), days	19.0 (± 17.7)	18.4 (±21.9)	0.46
ICU LOS- Mean (SD), days	11.9 (± 14.3)	11.0 (± 15.6)	0.10
30-day readmission – no. (%)	141 (12.9)	63 (3.9)	<0.01
In-hospital mortality – no. (%)	35 (3.2)	36 (2.2)	0.11
AKI – no. (%)	0 (0)	3 (0.2)	0.28
RRT - no. (%)	13 (1.2)	3 (0.2)	<0.01

Abbreviations: DOT, days of therapy

Table 3: Multivariate Analysis Evaluating Impact of Baseline Characteristics on the Primary Outcome

Term	Estimate	P Value
Post-intervention vs. pre-intervention	- 0.24	<0.01
Female sex	- 0.16	0.02
Age at encounter	- 0.01	<0.01
Time from ICU admission to antibiotic order	+ 0.04	<0.01
ID consult	+ 1.53	<0.01

Conclusion: This study assessed the impact of an ATO policy allowing 72 hours of empiric linezolid in the ICU. We found a statistically significant reduction in days of therapy of IVGP-AB without increases in LOS, mortality, readmission, and AKI.

Disclosures: **All Authors**: No reported disclosures

144. MSG-15: Pharmacokinetic (PK), Adverse Events (AEs), and Tolerability Data from an Open Label Randomized Clinical Trial (RCT) Comparing Oral Suba-itraconazole (SUBA-ITC) to Conventional Itraconazole (C-ITC) for Treatment of Endemic Mycosis (EM)

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Session: O-28. Innovations and Updates in Mycology

Background: C-ITC is a drug of choice for non-life-threatening, non-CNS histoplasmosis, blastomycosis, sporotrichosis, coccidioidomycosis and other EM. Oral C-ITC is problematic due to inconsistent absorption often leading to sub-therapeutic serum levels. SUBA-ITC is an FDA approved formulation which utilizes nanotechnology to provide more consistent absorption when compared to C-ITC. We performed an open-label RCT comparing SUBA-ITC to C-ITC for non-life-threatening non-CNS EM, and is the first US based RCT examining SUBA-ITC. Herein we report the PK during the first 6 wks of study therapy (rx) and drug-related AEs and tolerability throughout the course of rx.

Methods: Subjects with a proven or probable EM, who had received <14 days prior antifungal tx, and were able to take po meds were eligible. Those with life-threatening and CNS disease or prohibited meds were excluded. Subjects were randomized to SUBA-ITC 130 mg or C-ITC 200mg, both PO BID, for up to 6 mo. All subjects received loading doses x 3d. Clinical assessment was performed on d 7, 14, 28, 42, 84, and 180. PK and safety evaluations were performed on d 7, 14 and 42. Serum levels and AUC were calculated and demonstrated using combined ITC and hydroxy-ITC measurements. Tolerability was based on subject ability to remain on rx.

Results: 62 subjects are included in this analysis (31 each in SUBA-ITC and C-ITC, respectively). Median serum levels of ITC + hydroxy-ITC at d 7, 14 and 42 were consistently higher in the SUBA-ITC arm (Fig 1, p=0.8, NS). Combined AUC (ITC+hydroxy-ITC) were 2951 and 2845 for SUBA-ITC and C-ITC, respectively (NS). 4 subjects in each arm had sub-therapeutic d 7 levels (< 1000ng/ml). Drug-related AEs and tolerability were similar in both arms (Table 1). Lower extremity edema, hypertension, nausea, and anorexia were the most common AEs. Premature study withdrawal was seen in 12 (19%) subjects overall (5 and 7 subjects, respectively on SUBA-ITC and C-ITC).

Figure 1

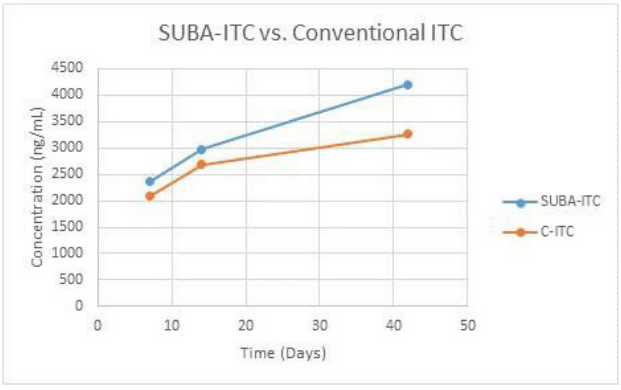

Table 1 Drug-Related Adverse Events (definite and probable) and withdrawals (tolerability)

Drug-related AEs	SUBA-ITC	Conventional ITC
Cardiovascular (edema, HBP, CHF, dyspnea)	9 (29%)	9 (29%)
Gastrointestinal (nausea, vomiting, abd pain)	4 (13%)	8 (26%)
Abnormal LFTs	1 (3%)	1 (3%)
Skin (alopecia)	0 (0%)	1 (3%)
Musculoskeletal	1 (3%)	0 (0%)
Early Withdrawals	5 (16%)	7 (23%)
Adverse event	3	3
Lack of efficacy	0	2
Pregnancy	0	1
LTFU	1	0
Withdrew consent	0	1
Unrelated death	1	0

Conclusion: SUBA-ITC dosed at 130 mg BID PO is safe, well-tolerated, and consistently leads to combined serum ITC/hydroxy-ITC levels and AUC that are higher (NS) when compared to C-ITC 200 mg BID. Moreover, compared to C-ITC, SUBA-ITC achieves these serum levels when administered at substantially lower daily doses (130mg BID vs 200 mg BID).

Disclosures: **Peter G. Pappas, MD**, **Mayne Pharma** (Scientific Research Study Investigator) **Andrej Spec, MD, MSCI**, **Mayne** (Consultant, Grant/Research Support) **Marisa H. Miceli, MD, FIDSA**, **SCYNEXIS, Inc.** (Advisor or Review Panel member)