Results. *K. pneumoniae* (n = 58; 48%) and *Enterobacter spp.* (n = 40; 33%) comprised the majority of CRE.

Table 1: CRE Susceptibility

Antimicrobials	EUCAST % Susceptibility (Breakpoint)	CLSI/FDA % Susceptibility (Breakpoint)	USCAST % Susceptibility (Breakpoint)	*P*-Value
Aminoglycosides				
Amikacin	66% (8)	86% (16)	55% (4)	<0.001
Gentamicin	21% (2)	31% (4)	21% (2)	<0.001
Tobramycin	15% (2)	18% (4)	14% (1)	0.063
Cyclines				
Minocycline	–	16% (4)	1% (1)	<0.001
Tigecycline	43% (1)	84% (2)	43% (1)	<0.001
Fluoroquinolones				
Levofloxacin	6% (0.5)	15% (2)	6% (0.5)	0.001

$P < 0.05$ are significant and indicate differences between CLSI/FDA and USCAST susceptibility.

Conclusion. Implementation of the proposed USCAST susceptibility breakpoints will impact clinician antimicrobial choice regarding the treatment of infections caused by CRE. Amikacin and tigecycline susceptibility markedly decreased when utilizing the proposed USCAST breakpoints.

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2431. Evaluation of Clinical Outcomes in Bacteremia Due to AmpC β-Lactamase Producing Organisms Stratified by Treatment

Travis Carlson, PharmD; Kady Phe, PharmD and Hannah Palmer Russo, PharmD; CHI St. Luke's Health - Baylor St. Luke's Medical Center, Houston, Texas

Session: 250. Treatment of AMR Infections

Saturday, October 6, 2018: 12:30 PM

Background. Enterobacteriaceae and *Pseudomonas aeruginosa* are common bloodstream pathogens with variable AmpC β-lactamase (AmpC) incidence. The clinical utility of treatment with non-carbapenem/cefepime options remains unclear. The objective of this study was to compare the clinical outcomes for patients receiving a carbapenem or cefepime (CC) and alternative therapy (AT) for bacteremia caused by organisms known to produce AmpC.

Methods. Hospitalized adults with a confirmed mono-microbial bacteremia admitted from June 2016 to December 2017 were included. Patients were stratified by definitive therapy (DT) with CC or AT. The AT group was treated with fluoroquinolones, third-generation cephalosporins, piperacillin–tazobactam, aztreonam, or tobramycin. The primary outcome was in-hospital mortality. Secondary outcomes included treatment failure, microbiological failure, hospital length of stay (LOS), and intensive care unit LOS. Multiple regression analysis was used to adjust for potential confounding variables.

Results. Of 68 patients meeting eligibility criteria, 46% received CC for DT. Enterobacteriaceae were isolated in 45% of patients in the CC group. In-hospital mortality was 32% and 3% (P = 0.0017) in the CC and AT groups, respectively. Source control, APACHE II score on the date of index culture, and immune status did not differ between groups. Definitive CC therapy was independently associated with mortality (odds ratio, 15.17; 95% confidence interval, 1.69–135.76; P = 0.0150). Only 6 (9%) patients received AT as empiric and DT. Those who received definitive AT received a median of 5 days (interquartile range, 3–9 days) of CC prior to being switched to AT.

Conclusion. While most patients received empiric CC, definitive treatment with CC was found to be an independent predictor of in-hospital mortality. These findings suggest that AT may be a de-escalation treatment strategy for clinicians to consider. However, these results should be confirmed in a larger population.

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2432. Appropriateness of Empiric Extended-Infusion Piperacillin/Tazobactam in the Intensive Care Unit

Kendall Tucker, PharmD[1]; Molly Benning, BS[2]; Keenan Ryan, PharmD, PhC[2]; Carla Walraven, PharmD, MS[2] and Bernadette Jakeman, PharmD, PhC, BCPS, AAHIVP[3]; [1]Pharmacy, University of New Mexico Hospitals, Albuquerque, New Mexico, [2]University of New Mexico Health Sciences Center, Albuquerque, New Mexico, [3]College of Pharmacy, University of New Mexico, Albuquerque, New Mexico

Session: 250. Treatment of AMR Infections

Saturday, October 6, 2018: 12:30 PM

Background. Gram-negative (GN) infections in ICU patients have increased antibiotic resistance owing to higher minimum inhibitory concentrations (MICs). Piperacillin/tazobactam (PTZ) 3.375 g extended infusion (EI) may be used as an empiric agent. GN organisms with PTZ MICs > 16/4 may not be adequately covered by this regimen. The objective of this study was to evaluate MICs of GN isolates from the ICU to determine whether PTZ 3.375 g EI is an appropriate empiric regimen for ICU patients. Appropriateness of empiric antibiotic therapy was defined as PTZ MIC ≤16/4 in greater than 80% of isolates. The secondary objective was to evaluate patient specific risk factors that may be associated with elevated PTZ MICs in GN pathogens.

Methods. All ICU patients admitted from January to December 2017 with a confirmed GN pathogen from a non-urinary source were included. Patients were excluded if they had cystic fibrosis, cultures obtained >48 hours prior to ICU admission, or they were incarcerated. Patients' electronic medical records were reviewed for the following data: age, sex, ethnicity, location prior to ICU admission, GN pathogen, culture source, risk factors for multi-drug-resistant organisms (dialysis, injection drug use, indwelling catheter, wounds/trauma), pathogen susceptibility profile, risk modifying co-morbidities (diabetes, heart failure, chronic kidney disease, and liver disease) and creatinine clearance.

Results. 231 patients were included in the study. The average patient was 56.7 years old ±16.95. The majority of patients were white (64.1%) and male (69.7%). There were no significant differences in baseline characteristics between patients with PTZ MICs >16/4 and those with MICs ≤16/4. *Pseudomonas aeruginosa* (41%) was the primary organism identified and 28% of all GN isolates had MICs >16/4. Dialysis (P = 0.028), IV antibiotics (P < 0.001) and presence of wounds or trauma (P = 0.018) were all associated with elevated MICs.

Conclusion. Current PTZ EI 3.375g dosing may not provide adequate empiric coverage of GN pathogens for ICU patients especially for patients who received previous IV antibiotics, are on dialysis, or have the presence of wounds or trauma.

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2433. Evaluation of Meropenem (MEM) in Combination With Colistin (COL) Against Colistin-Resistant Extensively Drug-Resistant (XRD) Gram-Negative Bacteria

Nivedita Singh, MS[1]; Logan Nguyen, Student[1]; Michael J. Rybak, PharmD, MPH, PhD[2] and Keith S. Kaye, MD, MPH[3]; [1]Pharmacy Practice, Anti-Infective Research laboratory, Department of pharmacy practice, Detroit, Michigan, [2]259 Mack Ave, Suit 4131, Eugene Applebaum College of Pharmacy and Health Sciences Bldg, 259 Mack Ave., Detroit, Michigan, [3]Internal Medicine, Division of Infectious Diseases, Michigan Medicine, Ann Arbor, Michigan

Session: 250. Treatment of AMR Infections

Saturday, October 6, 2018: 12:30 PM

Background. The treatment of XDR Gram-negative bacilli poses a significant clinical challenge with limited treatment options. Colistin-resistant XRD Gram-negative bacteria are becoming more commonplace in the clinical setting. Combination therapy is resorted to for treatment of such strains. The objective of this in-vitro study was to evaluate the synergistic effect of the combination with COL and MEM against Colistin-resistant XDR Gram-negative bacilli.

Methods. In this study, a total of 30 Colistin-resistant XDR Gram-negative clinical isolates were evaluated, including five isolates of Pseudomonas aeruginosa, twenty-four isolates of Acinetobacter baumannii and one isolate of Klebsiella pneumonia. Minimum inhibitory concentrations (MICs) were determined with COL and MEM for each strain by broth microdilution. COL and MEM MICs were measured in the presence of 0.25- to 0.5- × the MIC of the other antibiotic to determine the ability to lower MIC values. Time-kill assays were performed with each agent alone and in combination to evaluate the potential for synergistic interactions. Additive and synergistic effects were defined as 1- to 2-$\log_{10}$ and ≥ 2-$\log_{10}$ reductions in CFU/mL from the most active single agent at 24 hours, respectively.

Results. All isolates were resistant to COL (MIC90 32 mg/L), whereas all bacteria with except one A. baumannii, were resistant to MEM (MIC90 >64 mg/L). Zero- to greater than nine-fold decrease in MEM MICs were observed in combination with COL at 0.25- to 0.5 × MIC. COL MICs decreased by 0 to >8-fold when combined with MEM. MEM plus COL demonstrated synergistic activity against 70% strains tested and additive in 3% of the tested strains at 24 h in time-kill. The combination was indifferent in 26% of the tested strains.

Conclusion. These data indicate that the addition of MEM to COL therapy in colistin resistant XDR Gram-negative bacteria demonstrate synergistic or additive effects against a majority of XDR Gram-negative bacteria. The combination might be a promising therapeutic option for treatment of these problem pathogens.

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2434. Review of Linezolid (LZD) Use and Onset of Toxicity in 4 Belgian Hospital Centers: A Retrospective Study

Helene Thirot, PharmD[1]; Caroline Briquet, PharmD[2]; Frédéric Frippiat, MD[3]; Frederique Jacobs, MD[4]; Xavier Holemans, MD[5]; Paul Tulkens, MD[6]; Anne Spinewine, Pharm, PhD[1] and Francoise Van Bambeke, PharmD, PhD[7]; [1]Universite Catholique de Louvain, Brussels, Belgium, [2]Department of Pharmacy, Université Catholique de Louvain, Clinique Universitaires Saint Luc, Brussels, Belgium, [3]Infectious Diseases and Internal Medicine, Centre Hospitalier Universitaire

De Liège, Liège, Belgium, [4]Erasme University Hospital, Brussels, Belgium, [5]Grand Hopital de Charleroi, Charleroi, Belgium, [6]Université Catholique de Louvain, Bruxelles, Belgium, [7]Université Catholique de Louvain, Brussels, Belgium

Session: 250. Treatment of AMR Infections
Saturday, October 6, 2018: 12:30 PM

Background. LZD is approved (FDA label and Belgian Summary of Product Characteristics [SmPC]) for the treatment of SSSTI and pneumonia caused by Gram-positive organisms (mainly MRSA and VRE) only. Yet IDSA recommendations for MRSA infections also position LZD for osteomyelitis and as an alternative for CNS infections and bacteremia (CID 2011;52:e18–55). LZD use is limited by adverse events, the incidence of which may vary according to the length and conditions of therapy. The aim of this study was to document LZD actual use and onset of adverse events in real life clinical practice.

Methods. Observational, retrospective study in 4 Belgian hospital centers (about 4,000 beds) over 1 year (2016). Analysis of medical files (222 treatments) to collect information on (i) patient's characteristics and treatment modalities and indications, (ii) occurrence, causality and severity of adverse drug reactions (ADR), and (iii) concomitant medications (increasing the risk of developing a serotonin syndrome [SS]).

Results. Key data are shown in the figure. 18% of prescriptions matched the indications approved in the United States and in Belgium and 47% those mentioned in the IDSA recommendations. 54% of the patients were infected by bacteria resistant to first choice drugs. Decreases in platelet counts (DPC) were observed in 30% of patients (compared with <1% thrombocytopenia in the Belgian SmPC or 25% DPC in 3% of patients in FDA label) and was observed in 15/39 cases (patients with in-Belgian label indications), 35/105 cases (patients with IDSA indications), 30/117 (other indications). Treatment duration > 10 days was the only significant risk factor for DPC (Kaplan Meyer; $P < 0.005$ [Mann–Whitney]). 7 cases of CNS ADR were reported. Although 41% of patients were prescribed at least 1 drug increasing SS risk, SS was actually observed in only 1 patient.

Conclusion. LZD is mainly used in off-Belgian label indications, some of which, however, are in the IDSA recommendations. The high incidence of ADR (40%) as well as the frequent use of co-medications putting patients at risk of SS highlight the importance of follow-up for LZD-treated patients. A prospective study is now needed to better assess the severity of these ADR and identify more associated risk factors.

Patient's characteristics	**Values**
Number of patients	222
Male/Female	141/81
Age (year)	65 [21-95] [a]
Weight (kg)	77.3 [34-178] [a]
Renal function (GFR in mL/min)	58 [10-196] [a]
Treatment characteristics	**Values**
Oral route/ IV route, N	141/89
Posology	600 mg 2x/day
Treatment duration (days)	9 [1-90] [a]
Indications [b]	
Bacteremia, N (%)	44 (19.8)
Medical devices infections, N (%)	29 (13)
Skin and soft tissue infections, N (%)	25 (11.3)
Septicemia [c], N (%)	17 (7.6)
Osteitis, N (%)	16 (7.2)
Pneumonia, N (%)	14 (6.3)
Sepsis and Septic shock, N (%)	9 (4)
CNS infections, N (%)	6 (2.7)
Others, N (%)	62 (27.9)
Organisms	
Vancomycin-susceptible *E. faecium,* N (%)	61 (26.3)
Methicillin-resistant *S. epidermidis,* N (%)	58 (25)
Methicillin-resistant *S. aureus*, N (%)	42 (18.1)
Vancomycin-resistant enterococci, N (%)	20 (8.6)
Methicillin-susceptible *S. aureus,* N (%)	12 (5.2)
Methicillin-susceptible *S. epidermidis,* N (%)	2 (0.9)
Others, N (%)	37 (16)
Side effects	**N (%)**
Thrombocytopenia N (%) [b,d]	14 (6.3)
Decrease > 25% in blood platelets count N (%) [e]	66 (29.7)
Anemia N (%) [b]	6 (2.7)
Decrease > 25% of hemoglobin [e]	14 (6.3)
Peripheral neuropathy, N (%)	4 (1.8)
Paresthesia, N (%)	3 (1.4)
Serotonin syndrome, N (%)	1 (0.45)
Concomitant medication	**N (%)**
Tramadol	50 (21.9)
Selective serotonin reuptake inhibitor	21 (9.2)
Trazodone	14 (6.1)
Mirtazapine	10 (4.4)
Non selective monoamine reuptake inhibitor	9 (3.9)
Tricyclic antidepressant	4 (1.7)

[a] Median [range]
[b] As reported in the medical file
[c] in most of the cases, secondary to another infection
[d] value lower than the reference range in the corresponding hospital
[e] Definition of thrombocytopenia/anemia as mentioned in the US label

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2435. Clinical Outcomes With Ceftolozane–Tazobactam in Patients With Multidrug-Resistant (MDR) *Pseudomonas aeruginosa* Bloodstream Infections: A Multi-Center Study

Madeline King, PharmD[1]; Abdulrahman Elabor, MD[2]; Esther Molnar, MD[2]; Jason Gallagher, PharmD, FCCP, FIDSA, BCPS and TOL-TAZ for Resistant Pseudomonas Study Group; [1]Philadelphia College of Pharmacy, University of the Sciences, Philadelphia, Pennsylvania, [2]Infectious Diseases, Temple University Hospital, Philadelphia, Pennsylvania, [3]Temple University School of Pharmacy, Philadelphia, Pennsylvania

Session: 250. Treatment of AMR Infections
Saturday, October 6, 2018: 12:30 PM

Background. Ceftolozane-tazobactam (TOL-TAZ) is a novel cephalosporin combination that is beneficial for the treatment of multidrug-resistant (MDR) *Pseudomonas* infections. However, little data are available on the utility of TOL-TAZ for patients with bloodstream infections (BSIs) caused by this organism.

Methods. A retrospective, multicenter chart review was conducted at 11 hospitals to evaluate the utility of TOL-TAZ for MDR *Pseudomonas* BSIs from June 2016 to February 2018. Patients were included if they were over 18 years old with positive blood cultures for *Pseudomonas aeruginosa* and received TOL-TAZ for at least 24 hours. Patients were evaluated for in-hospital and 30-day mortality, as well as microbiologic and clinical cure.

Results.

Characteristic	Results (*N* = 25)
Male gender, *n* (%)	15 (60)
Age, median (range)	60 (52–66)
Charlson comorbidity index, median (IQR)	5 (4–7)
APACHE II score, median (IQR)	19 (16.25–25.5)
ICU, *n* (%)	15 (60)
Organ transplant, *n* (%)	8 (32)
Concomitant antibiotics used, *n* (%)	14 (56)
Aminoglycoside, *n*/*N* (%)	8/14 (57)
Fluoroquinolone, *n*/*N* (%)	5/14 (35)
Polymyxin, *n*/*N* (%)	2/14 (14)
β-Lactam, *n*/*N* (%)	1/14 (7)
Duration of TOL-TAZ, days (median, IQR)	13 (8-14)
Susceptibility to TOL-TAZ, *n*/*N* tested (%)	19/20 (95)
High dose (3g every 8 hours), *n* (%)	6 (24)
Renal dose adjustment, *n* (%)	8 (32)
Adverse events, *n* (%)	1 (4)

Primary infection	30 day mortality, *n*/*N* (%)	In-hospital mortality, *n*/*N* (%)	Microbiologic success, *n*/*N* (%)	Clinical Success, n/N (%)
Primary bacteremia	1/7 (14.3)	0/7 (0)	7/7 (100)	6/7 (85.7)
Pneumonia	5/8 (62.5)	5/8 (62.5	3/8 (37.5)	3/8 (37.5)
UTI	1/6 (16.7)	1/6 (16.7)	6/6 (100)	6/6 (100)
Intra-abdominal	0/4 (0)	0/4 (0)	4/4 (100)	4/4 (100)

30 day mortality, n (%)	7 (28)
In hospital mortality, *n* (%)	6 (24)
Microbiologic cure, *n* (%)	20 (80)
Clinical success, *n* (%)	19 (76)

Conclusion. In this multi-center evaluation of 25 patients from 11 health centers, mortality was seen at 30 days and at the end of stay in 28% and 24% of patients, respectively. Clinical and microbiologic success occurred in over 70% of patients. One patient developed *C. difficile* infection. The 7 patients with primary bacteremia had microbiologic success and survived their hospital stay. Two of 3 patients with pneumonia who survived received high dose TOL-TAZ. TOL-TAZ is an option for patients with MDR *Pseudomonas* bloodstream infections.

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