2445. Efficacy and Tolerability of Linezolid for Treatment of Infectious Spondylitis
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Background. Infectious spondylitis requires long-term antibiotic treatment for 6 weeks or more, and the use of intravenous antibiotics during this period causes social loss and costs due to hospitalization. Linezolid has high oral bioavailability and is not affected by changes in renal or hepatic function. We investigated the clinical and microbiological effects of linezolid in infectious spondylitis caused by β-lactam-resistant Gram-positive bacteria.
Methods. Clinical data about patients who were diagnosed infectious spondylitis and treated with linezolid for more than 4 weeks were collected by electronic medical record retrospectively at 3 tertiary hospitals from 2006 to 2016. Clinical and microbiological success of treatment were determined using medical record or bacterial culture results identified in blood or tissue.
Results. Twenty Korean cases were treated with linezolid more than 4 weeks during the study period. Median duration of linezolid treatment was 40.5 days. Major causative organism was methicillin-resistant Staphylococcus aureus (n = 15), followed by methicillin-resistant coagulase-negative Staphylococcus (n = 3). In 10 of 20 patients treated with linezolid, antibiotics were changed for side effects or de-escalation of antibiotics. The most common reason for discontinuation of linezolid was thrombocytopenia (n = 6). Fourteen patients were cured, 4 failed and 2 cases of mortality occurred due to other causes than infectious spondylitis. Nine of 13 patients who were assessed as vancomycin treatment failure were cured.
Conclusion. Linezolid can be used as an effective antibiotic agent in patients with infectious spondylitis, especially when treatment failure of the first-line treatment is expected. Linezolid can be administered orally in outpatient clinic, reducing healthcare cost. Since cytopenia (especially thrombocytopenia) are common, a regular follow-up of complete blood cell count is needed.
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2446. Clinical Spectrum and Outcomes of Collistin-Resistant Carbenapenem-Resistant Enterobacteriaceae
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Background. Collistin is considered as one of the last resort of antibiotics against carbapenem-resistant enterobacteriaceae. During the last decade, increased use of colistin or polymyxins due to the increasing prevalence of carbapenem-resistant Gram-negative bacteria has unfortunately led to the emergence of colistin-resistant strains. There are no defined antibiotic regimens for colistin-resistant strains which makes the treatment of these organisms extremely challenging. We therefore report the clinical spectrum and outcomes of infections due to colistin-resistant carbapenem-resistant Enterobacteriaceae (Co-CRE) as well as the factors associated with acquisition of Co-CRE.
Methods. We conducted a retrospective cross-sectional study from January 2013 till December 2017 on patients admitted to a tertiary care hospital in Karachi, Pakistan. Statistical analysis was done using SPSS 19.
Results. Forty patients with Co-CRE were identified of which 29 (72.5%) were males, Median age was 54.5 years. The most common organism isolated was Klebsiella in 25 (55%) followed by Providencia. Most common site of infection was the lung in 12 (30%) followed by urine in 11 (27.5%) patients. Similarly, the most common cause of bacteremia was pneumonia followed by intra-abdominal infections (50% and 37.5% of bacteremia cases, respectively). Eighty-two (70%) patients had prior cultures with multi-drug-resistant organisms and 36 (90%) had used antibiotics in the past. A quarter (10) patients had pan resistant co-CRE strains while of the remaining strains 66% were sensitive to Fosfomycin. All patients received Colistin-based regimen in combination with 2 or 3 of the following: carbapenem, Fosfomycin, Amikacin, co-triamoxazole, and tigecycline. Complete clinical cure was achieved in only 50% of patients whereas microbiological eradication was achieved in 75%. Higher PITT bacteremia score, solid-organ transplant, and acute kidney injury were associated with mortality in patients with co-CRE.
Conclusion. Infections with co-CRE were seen in patients with prior nosocomial exposures and led to poor outcomes, despite combination treatment guided by susceptibilities.
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Methods. A total of 7,037 non-duplicate Eba were collected from UTI, IAI, or LRTI in 26 sites in 6 countries in LA, as a part of the INFORM surveillance study from 2012 to 2016. Susceptibility testing was by broth microdilution using CLSI 2018 breakpoints. CAZ-AVI was tested with a fixed concentration of 4 μg/mL avibactam. Meropenem nonsusceptibility prompted β-lactamase screening by PCR and sequencing.

Results. CAZ-AVI demonstrated potent in vitro activity against Eha from UTIs, IAs and LRTIs (99.6%, 99.8%, and 99.5% susceptible, respectively). CAZ-AVI was active against colistin-resistant and MDR Eba as well as meropenem-nonsusceptible Eba not encoding metallo-β-lactamases (96.5%, 98.4% and 94.4% susceptible, respectively) (Table).

| Phenotype      | All (%) | UTI (%) | IAI (%) | LRTI (%) |
|----------------|---------|---------|---------|----------|
| Eba, All       | 99.6% (7037) | 99.8% (2,918) | 99.8% (2,401) | 99.5% (1,718) |
| CAZ-AVI        | 98.7% (7,110) | 98.4% (3,793) | 99.2% (3,079) | 98.5% (2,604) |
| MEM-NS         | 93.8% (372) | 92.3% (147) | 95.7% (116) | 92.7% (109) |
| MEM-NS, MBL-negative | 99.4% (351) | 99.3% (138) | 99.1% (110) | 100% (101) |
| CST-R          | 96.5% (144) | 98.4% (63) | 97.3% (37) | 93.2% (44) |
| MDR            | 98.4% (1,458) | 98.1% (591) | 98.8% (480) | 98.2% (385) |

Infection source: UTI; urinary tract; IAI, intra-abdominal tract; LRTI, lower respiratory tract. CAZ-AVI, ceftazidime–avibactam; CAZ, ceftazidime; MEM, meropenem; CST, colistin; MDR, multidrug-resistant; MBL, metallo-β-lactamase; NS, nonsusceptible; R, resistant.

Conclusion. CAZ-AVI exhibited potent in vitro activity against Eha from UTIs, IAs and LRTIs isolated in Latin America from 2012 to 2016 and provides a vital alternative to colistin and meropenem when MBLSs are not present.

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2449. Validation of In Vitro Activity of Aminoglycosides Against Recently Isolated Helicobacter pylori for the Commercialization of Gentamicin-Intercalated Smectite Hybrid as a New Therapeutic Agent

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Background. The eradication rate of Helicobacter pylori as a standard therapy based on a standard regimen of eradicating H. pylori, exhibits a decreasing trend. Alternative approaches have been explored, but there is still controversy in the regimen change and these do not provide a satisfactory substitute to the existing standard therapy. Thus, a novel and efficient H. pylori eradication regimen should be developed. Smeccite can serve as a drug delivery system and gentamicin intercalated smectite hybrids (S-GEN) are expected to supersede the standard therapy for H. pylori eradication. In the previous study, we synthesized S GEN complexes as a novel therapeutic agent. In a murine model, S GEN released gentamicin to the gastric wall stably and the therapeutic effect was not inferior to the conventional standard therapy. The aim of this study was to confirm whether the minimum inhibitory concentration (MIC) of aminoglycosides applied as smectite hybrids remained low against recently isolated H. pylori strains.

Methods. The H. pylori strains were collected via endoscopic biopsy from 1,422 patients at Gangnam Severance Hospital in Seoul, Korea, between March 2015 and February 2018. Antimicrobial susceptibility tests were performed, and the MICs of eight antibiotics (amoxicillin, clarithromycin, metronidazole, tetracycline, levofloxacin, which are alternative therapies for H. pylori eradication. In clarithromycin-resistant strains, the MIC was 0.25 mg/L and the MIC, was 1 mg/L for gentamicin; for nitrofurantoin, the values were 0.25 mg/L and 0.75 mg/L, respectively.

Conclusion. Through the use of gentamicin and netilmicin, which have low MICs for H. pylori, aminoglycoside-intercalated smectite hybrids are expected to emerge as a new standard therapy for H. pylori eradication.

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2450. Antibiotic Treatment for Carbapenem-Resistant Enterobacteriaceae (CRE) and Outcomes in Veterans With Spinal Cord Injury/Disorder (SCI/D) Monti, D; Little, P; PharmD; Ursula, C; PharmD; RCS, K; and HYPY, K; Katie J. Suda, PharmD, MS; Margaret Fitzpatrick, MD, MS; and Charlesnka T. Evans, PhD, MPH

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Background. A total of 282,000 people (17% veterans) in the United States have SCI/D. Infection is a significant source of morbidity and the leading cause of death in this population. Due to frequent healthcare contact and antibiotic use, SCI/D is associated with high risk of multidrug-resistant infections, including CRE. CRE are resistant to most antibiotics and associated with high mortality. The objective of this study was to describe antibiotics used for CRE infection and clinical outcomes in veterans with SCI/D.

Methods. This retrospective cohort used national VA data of veterans with SCI/D and active CRE infection (per documentation in the health record) from 2011 to 2013. CRE was defined as resistant to a carbapenem and third generation cephalosporin. Antibiotics were described by empiric/definitive and monotherapy/combination therapy. Clinical outcomes included clinical failure/improvement, microbiological resolution, mortality and readmission. One-year follow-up data for patients with a second MIC was analyzed for use with significance at p ≤ 0.0125 due to multiple comparisons.

Results. Ninety-two CRE infections (62% K. pneumoniae) were identified in 87 patients, most often in urine cultures (58.7%). Carbapenems (20.7%) were used most commonly for CRE treatment, followed by combination therapy with aminoglycosides (earlier or definitive therapy). Definitive combinations consisted of carbapenems/polymyxins (16.7%) or carbapenems/aminoglycosides (13.3%). Clinical outcomes for definitive monotherapy vs. combination, respectively, were: clinical failure (26.6% vs. 46.7%), improvement 1–10 days (43.2% vs. 33.3%), and 11–30 days (70.4% vs. 53.3%); microbiological resolution (48.2% vs. 38.8%); mortality at 30 days (22.2% vs. 30%), 90 days (22.2% vs. 41.7%), 1 year (25.9% vs. 51.7%) and readmission at 30 days (11.1% vs. 10%) and 1 year (37% vs. 30%). No significant differences in outcomes were identified for monotherapy vs. combination therapy or susceptible vs. non-susceptible treatment.

Conclusion. For CRE treatment in the SCI/D population, carbapenems were the most widely used drug class; combination therapy was used most frequently. No improvements in clinical outcomes were found for combination therapy as either empiric or definitive treatment or compared to susceptible or susceptible treatable.

Disclosures. All authors: No reported disclosures.

2451. Synergistic Activity of Ceftazidime–Avibactam in Combination With Polymyxin B Against Carbapenem-Resistant Klebsiella pneumoniae Jovan Borjan, PharmD and Eric Wenzler, PharmD; College of Pharmacy, University of Illinois at Chicago, Chicago, Illinois

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Background. Combination antimicrobial therapy is often recommended for the treatment of serious infections due to carbapenem-resistant Klebsiella pneumoniae (CRKP). Demonstrating synergy between ceftazidime–avibactam (C-A) and other antimicrobials in vitro may help elucidate the rate, magnitude, and duration of bacterial activity and suggest combinations that may be effective in the clinical arena. Methods. Three clinical CRKP were used for all experiments. C. A and polymyxin B (PB) MICs and time-kill analyses were performed in triplicate according to CLSI guidelines. Individual drugs were tested at ¼, ½, 1, 2, 4x MIC. A 23 log CFU/mL reduction compared with the starting inoculum (107) was considered bactericidal. Results. Three clinical CRKP were used for all experiments. C. A and polymyxin B (PB) MICs and time-kill analyses were performed in triplicate according to CLSI guidelines. Individual drugs were tested at ¼, ½, 1, 2, 4x MIC. A 23 log CFU/mL reduction compared with the starting inoculum (107) was considered bactericidal. In contrast, bactericidal activity was observed at 24h with C-A alone at ½ MIC and in combination at ¼ MIC (3.4 and 3.6 log CFU/mL reduction, respectively) for strain KPC3. Synergy was not observed for any isolate at the concentrations tested.

Conclusion. C-A demonstrated concentration-dependent bacterial activity against all CRKP whereas PB showed initial bactericidal follow by regrowth and development of resistance. The combination of C-A and PB was not synergistic against C-A and PB susceptible or resistant CRKP isolates. Our data do not support the use of ceftazidime–avibactam in combination with polymyxin B for CRKP.