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

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

Background. The eradication rate of Helicobacter pylori as a standard therapy based on conventional antibiotics in Asian countries, 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. Smedicate 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 superior to 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, gentamicin, netilmicin, and tobramycin) were determined by using the Etest method and following the European Committee on Antimicrobial Susceptibility Testing recommendations.

Results. Finally, 140 H. pylori strains were analyzed in this study. The resistance rate to clarithromycin was 30.7%, although it is a major antimicrobial agent used in standard therapy. The MICs and MICs of gentamicin (MIC, 0.25 mg/L and the MIC, 0.9 mg/L, MIC, 0.75 mg/L) were lower than that of metronidazole, tetracycline and levofloxacin, which are alternative therapies for H. pylori eradication. In clarithromycin-resistant strains, the MIC of was 0.25 mg/L, and the MIC, 0.9 mg/L, for netilmicin, 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.

Disclosures. All authors: No reported disclosures.

2450. Antibiotic Treatment for Carbapenem-Resistant Enterobacteriaceae (CRE) and Outcomes in Veterans With Spinal Cord Injury/Disorder (SCI/D) Patient Treatment, PharmD; Ursula Charles, PharmD; RP, BCPS; Katie J. Suda, PharmD, MS,E1; Margaret Fitzpatrick, MD, MS1 and Charlesen T. Evans, PhD, MPH2.

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

Background. A total of 282,000 people (17% veterans) in the United States have SCI/D. CRE 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 rate. Piperacillin-tazobactam (P-1 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 frequently for CRE treatment. Combination therapy was used more often than monotherapy (empiric 56.3%, definitive 69.0%). Definitive combinations consisted of carbapenems/polyoxins (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 (48.2% vs. 33.3%), and 11–30 days (70.4% vs. 53.3%); microbiological resolution (48.2% vs. 38.3%); 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 as susceptible or non-susceptible treatment.

Disclosures. All authors: No reported disclosures.

2451. Synergistic Activity of Ceftazidime–Avibactam in Combination With Polymyxin B Against Carbapenem-Resistant Klebsiella pneumoniae

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

Background. Combination antimicrobial therapy is often recommended for the treatment of multi-drug resistant K. pneumoniae (CRKP). Demonstrating synergy between ceftazidime–avibactam (C-A) and other antimicrobials in vitro may help elucidate the rate, magnitude, and duration of bactericidal 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 log10 CFU/mL reduction compared with the starting inoculum (107) was considered bactericidal. Synergy was assessed by testing combinations at the highest concentration of each drug that showed no activity alone and was defined as 22 log10 CFU/mL increase in killing at the combination with compared most with active agent alone.

Results. MICs: C-A 1, 8, 16, 32 mg/L; PB 0.25, 0.5, 64 mg/L. C-A alone was bactericidal against all strains at 4x MIC (mean 24 hours bacterial reduction of 3.42 log10 CFU/mL). PB at 4x MIC was bactericidal for all strains at 6 hours (mean bacterial reduction of 3.58 log10 CFU/mL) but regrowth to control levels was seen at 24 hours. C-A alone at ¼ MIC and combinations at ¼ MIC for strains KP1 and KP2 yielded minimal killing followed by regrowth (mean 24 hours total bacterial count of 8.77 log10 CFU/mL). In contrast, bactericidal activity was observed at 24h with C-A alone at ¼ MIC and in combination at ¼ MIC (3.14 and 3.62 log10 CFU/mL reduction, respectively) for strain KP3. Synergy was not observed for any isolate at the concentrations tested.

Conclusion. C-A demonstrated concentration-dependent bactericidal activity against all CRKP whereas PB showed initial bactericidal follows 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.