including vancomycin intermediate susceptible *Staphylococcus aureus* (VISA) and daptomycin non-susceptible strains (DNS). Lipoglycopeptides; notably dalbavancin (DAL), have been employed due to their ease of administration and enhanced activity against highly resistant *S. aureus*. As previously demonstrated, the use of β-lactams, specifically cefazolin (CFZ) in combination with anti-MRSA drug therapy has been effective in eradicating *S. aureus* complicated by increased resistance. The objective of this study was to evaluate the activity of DAL, VAN, and DAP, alone and in combination with CFZ in a pharmacokinetic/pharmacodynamic (PK/PD) model.

Methods. The well-characterized DNS-VISA strain, D712, was evaluated in eight different regimens in duplicate via a one-compartment 7-day PK/PD model. The experimental regimens were as follows: D712 growth control, DAL 1500 mg given on day 1, VAN 2 g given every 12 hours, DAP 10 mg/kg once-daily, CFZ 2 g given every 8 hours and DAL, DAP, and VAN in combination with CFZ.

Results. The combinations of DAL+CFZ, VAN+CFZ, and DAP+CFZ demonstrated a significant $\log_{10}$ CFU/mL reduction (more than 5 $\log_{10}$ CFU/mL and up to detection limit), compared with each drug used as monotherapy ($P < 0.001$). Neither DAP nor VAN demonstrated sustained bactericidal activity, (represented by a >3-$\log_{10}$ CFU/mL reduction from baseline) and resulted in significant regrowth, when administered alone. However, the DAP +CFZ, and VAN+CFZ combination models demonstrated bactericidal activity at 4 hours and 24 hours, respectively. While DAL alone did demonstrate bactericidal activity, the DAL+CFZ combination was more rapidly bactericidal, achieving a > 3-log reduction from baseline in 8 hours vs. 48 hours ($P < 0.05$).

Conclusion. The combination of DAL, VAN, or DAP with CFZ demonstrated significantly improved activity against this multiple drug-resistant *S. aureus* strain. Further research is warranted, both *in vivo* and *in vitro*, to explore the synergistic capabilities of anti-MRSA drug therapy in combination with β-lactams.

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1540. A Population Pharmacokinetic Model for Vancomycin in Korean Patients Receiving Extracorporeal Membrane Oxygenation Therapy: A Prospective Study

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Background. There is no literature on population pharmacokinetics (PK) of vancomycin in Korean patients receiving extracorporeal membrane oxygenation (ECMO) therapy. The aim of this study was to develop a population PK model for vancomycin in Korean ECMO patients.

Methods. We prospectively enrolled adult patients who were undergoing ECMO and receiving vancomycin from July 2018 to April 2019. After initial dose of vancomycin was administrated, serial blood samples (seven to nine times per patient) were drawn before the next dose. A population PK model for vancomycin was developed using a nonlinear mixed-effect modeling. Age, sex, creatinine clearance, and body weight were tested as potential covariates in the model. Model selection was based on log-likelihood test, model diagnostic plots, and clinical plausibility.

Results. Fourteen patients were included over the period. Ten received venovenous, three venoarterial, and one both type ECMO. Eleven were men and the median age was 54 (interquartile range 45–66.3). Mean estimated glomerular filtration rate (eGFR) was 69 ± 46 mL/minute/1.73m^2 by the modification of diet in renal disease equation. A total of 123 vancomycin concentrations from the patients were included in the analysis. The population PK of vancomycin was best described by a two-compartment model with a proportional residual error model. The typical value (%between-subject variability) for total clearance was estimated to be 4.33 L/h (21.6%), central volume of distribution was 9.22 L, the intercompartmental clearance was 10.75 L/hr (34.9%) and the peripheral volume of distribution was 19.6 L (26.6%). The proportional residual variability was 8.81%. Creatinine clearance significantly influenced vancomycin clearance (CL). The proposed equation to estimate vancomycin clearance in Korean ECMO patients was CL = 4.33 + 0.199 × (eGFR – 56).

Conclusion. A two-compartment population PK model successfully describes vancomycin PK profiles in Korean ECMO patients. The model could be used to optimize the dosing regimen if more data become available from currently ongoing clinical study.

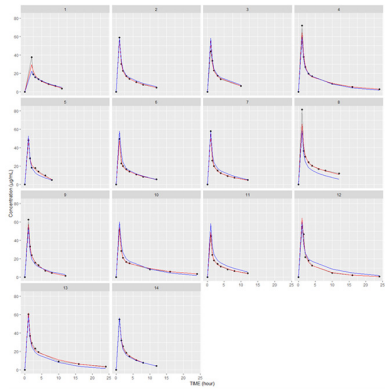

Fig. Individual fit plots (dots and black lines, observed individual concentrations; red lines, individual predicted concentrations; blue lines, population predicted concentrations)

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1541. A Novel and Fast Liquid Chromatography Method for Determination of Fluoroquinolones in Human Plasma

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Background. Fluoroquinolones (FQs) are frequently used antimicrobial agents. Considering that the FQs exhibit concentration-dependent bactericidal activity, concentrations of FQs in the biological fluids must be monitored to ensure treatment success. The literature search revealed that there is no method for the determination of levofloxacin (LEV), ciprofloxacin (CIP), moxifloxacin (MOX), and gemifloxacin (GEM) in plasma up to date. Consequently, the aim of this study was to develop and validate a new high-performance liquid chromatography (HPLC) method for determination of these FQs in plasma and evaluate effects of concomitant drugs on plasma FQ concentrations of patients.

Methods. Blank plasma samples spiked with FQs were employed for method validation studies. Validation studies were conducted in accordance with the recommendations of the US FDA. In order to demonstrate feasibility of method, 5 patients with polypharmacy, receiving orally CIP, LEV, or MOX as part of their treatment were included in the study. Blood samples were collected at two different times, just before and 2 hours after the second drug administration.

Results. The separation of FQs was accomplished within 7.5 minutes. The method was linear in the range of 0.1–10 μg/mL with the correlation coefficient >0.99. The RSD at four concentration levels (0.1, 0.3, 4, and 8 μg/mL) was less than 7% with accuracy in the range of 91.8–111.9%.The method was applied to the determination of CIP, LEV, and MOX levels in plasma samples of 5 patients with polypharmacy. Determined CIP and LEV levels were in accordance with literature. On the other hand, MOX concentration 2 hours after administration in plasma of one patient was found to be 6.1 ± 0.1 μg/mL which was higher than previously reported maximum plasma concentration of MOX (4.5 μg/mL). The patient had hypoalbuminemia and MOX is approximately 50% bound to serum proteins. Due to low level of albumin, the level of free MOX in plasma may be increased.

Conclusion. A simple, fast, and reliable HPLC method was developed and validated for the determination of LEV, CIP, MOX, and GEM in plasma. It is suitable therapeutic drug monitoring of these FQs and can be applied to other pharmacokinetic and toxicological studies.

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1542. The Evaluation of the *In Vitro* Synergy of Colistin in Combination with Meropenem and Tigecycline against 50 Multi-Drug-resistant *Acinetobacter baumannii* strains

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Background. *Acinetobacter baumannii* possess inherent and acquired antibiotic resistance mechanisms that have rendered most antibiotics, including carbapenems, inactive. Colistin (COL) has risen as salvage therapy against these organisms due to its retained activity against *A. baumannii*. However, COL monotherapy is often met with suboptimal outcomes. Recently, combination therapy with COL and meropenem (MEM) or tigecycline (TGC) has been shown to be effective in eradicating multi-drug-resistant *A. baumannii* infections. The objective of this study was to further evaluate the efficacy of COL in combination with MEM or TGC against 50 multi-drug-resistant *A. baumannii* strains.

Methods. Fifty carbapenem-resistant *A. baumannii* strains were evaluated using combination minimum inhibitory concentration (MIC) testing and time-kill analysis (TKA). Single-drug MIC testing was performed for each strain by broth microdilution. Combination MIC testing was performed for COL+MEM and COL+TGC. Each strain was evaluated via 24-hour TKA to assess the synergistic capabilities of COL+MEM, and COL+TGC. Synergy was defined as a ≥ 2-log reduction CFU/mL in either combination from the most active single agent, while bactericidal activity was defined as a ≥ 3-log reduction CFU/mL of either combination from the initial inoculum.

Results. All 50 strains were resistant to MEM and TGC with MICs ≥ 64 μg/mL and ≥ 4 μg/mL respectively; while 3 strains were resistant to COL, MICs ≥ 2 μg/mL. MEM and TGC MIC values were reduced as much as 128-fold (median 2-fold) and 32-fold (median 2-fold),, respectively, in the presence of subinhibitory COL. COL MIC values were reduced as much as 512-fold (median 4-fold) from baseline in the presence of subinhibitory MEM, and as high as 16-fold (median 2-fold) in the presence of TGC. In TKAs, COL+MEM was synergistic in 45/50 (90%) strains and bactericidal against 43/50 (86%) strains. COL+TGC TKAs revealed synergy in 32/50 (64%) strains, and bactericidal activity against 28/50 (56%) strains.

Conclusion. The combinations of COL+MEM and COL+TGC demonstrate promise in combating highly resistant *A. baumannii*. Further research is mandated to explore other combinations that are capable of eradicating multi-drug-resistant *A. baumannii*.

Disclosures. **All authors:** No reported disclosures.