EV0003

ePoster Viewing

Antimicrobials: antibiotic usage

Quantitative assessment of the combination of doripenem or tigecycline with amikacin therapy against an isolate of carbapenemase-producing *Klebsiella pneumoniae* using drug interaction modelling

A. Farkas[1,2], C. Hoffman[3], M. Zeolla[2], N.R. Chin[4]

[1]*Optimum Dosing Strategies, Bloomingdale- NJ, USA*

[2]*Vassar Brothers Medical Center, Poughkeepsie- NY, USA*

[3]*Nyack Hospital, Nyack- NY, USA*

[4]*Touro College of Pharmacy, New York- NY, USA*

Background. Combination antimicrobial therapy is a strongly recommended strategy to control multidrug-resistant bacterial infections. Selection of antibiotic combinations is usually empirical, and conventional assessment of combined drug effect is rarely conducted to support selection of appropriate treatment regimens. Here, we report the results of a quantitative method to assess combined killing of antimicrobial agents to support selection of a treatment regimen against a clinical isolate of carbapenemase producing *Klepbsiella pneumoniae* (KPC).

Methods. Checkerboard studies were performed using clinically achievable concentrations for the combination of amikacin with doripenem and amikacin with tygecycline in 5 by 8 and 6 by 6 designs, respectively. Susceptibility profile of the isolate was established by Vitek 2. Bacterial burden observed at 24 h was mathematically modeled using a 3-dimensional response surface model of Greco and Bayesian methods. The established alpha interaction parameters and respective 95% confidence intervals (95% CI) were used to classify regimens into categories of synergistic, additive, or antagonistic effect.

Results. MIC measurements showed values susceptible to amikacin and tigecycline, while resistant to doripenem. The two antimicrobial combinations were found to have different efficacy against the multidrug resistant bacteria. As predicted by this method, doripenem plus amikacin was found to be the superior combination, which was evidenced by a greater reduction in bacterial burden during the 24 h experiment. Resulted alpha (95% CI) interaction parameters of 1.55 (1.04,1.97) indicated synergy and -2.51 (-2.97,-2.02) inferred antagonistic effect for the combination of doripenem with amikacin and tigecycline with amikacin, respectively.

Conclusions. This modeling approach is a robust method in evaluating the effectiveness of different combinations of antibiotics against KPC isolates. Amikacin with doripenem was the more effective combination in this in vitro model. Despite the favorable susceptibility profiles of tigecycline, its combination with amikacin may result in antagonism, thus empiric selection of this dual therapy should be avoided.