EV0466
ePoster Viewing
Diagnostic bacteriology – culture based

Interactions of tigecycline with colistin, gentamicin or meropenem against tigecycline resistant carbapenemase producing Klebsiella pneumoniae isolates

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Background: Over the last decade, carbapenemase producing Klebsiella pneumoniae isolates have become increasingly common worldwide, while infections related to them have been associated with therapeutic failures and high mortality rates. Meropenem, tigecycline, colistin and gentamicin are being used as last resort drugs, but increasing resistance rates have been often rendering them inactive. The therapeutic inadequacy has led to drug combination studies. We assessed the in vitro effectiveness of binary combinations of tigecycline with colistin, gentamicin or meropenem against tigecycline resistant carbapenemase-producing Klebsiella pneumoniae isolates, often resistant to the rest of the agents tested, using time-kill methodology**.**

Material/methods: Susceptibility testing was performed by the semi-automated VITEK 2 system as a screening method and MICs for all antimicrobials involved were confirmed with the Etest. Resistance mechanisms to carbapenems were phenotypically detected according to the EUCAST guidelines. Interactions between tigecycline and colistin, gentamicin or meropenem were assayed by the time-kill methodology. Synergy was defined as a ≥2-log10 decrease in cfu/ml between the combination and the most active single agent at various time intervals (1, 3, 5 and 24h). Antagonism was defined as a ≥2-log10 increase in cfu/ml between the combination and the most active single agent, while all other interactions were characterized as indifferent. Clinically achievable fixed agent concentrations were used

Results: A total of 24 carbapenemase producing Klebsiella pneumoniae isolates were used and 48 combinations between tigecycline and either colistin, gentamicin or meropenem were evaluated. All isolates tested were resistant to tigecycline with MICs 4 – 12 mg/L. The combination of tigecycline/colistin exhibited synergy for 5 of 12 (41.7%) colistin resistant isolates mostly at 5h and for 2 of the 8 (25%) colistin susceptible isolates at 24h. In one of the 12 (8.3%) colistin resistant and in one of the 8 (12.5%) colistin susceptible isolates an antagonistic interaction was observed after exposure to the combination of tigecycline/colistin. The combination of tigecycline with gentamicin was synergistic in one of the 10 gentamicin resistant isolates (10%) and in 2 of the 8 susceptible isolates (25%). All 10 interactions between tigecycline and meropenem were indifferent.

Conclusions: This study demonstrates the possibility of synergistic interaction of tigecycline and colistin against K.pneumoniae strains resistant to both agents, an important observation for the clinician, deserving routine testing as well as further evaluation with a greater number of strains.