27th ECCMID Vienna, Austria 22 – 25 April 2017
The congress of ESCMID

Session: EV023 Pharmacoepidemiology, improved prescribing and antibiotic stewardship

Category: 5b. Pharmacokinetics/pharmacodynamics of antibacterial drugs & therapeutic drug monitoring

22 April 2017, 08:45 - 15:30
EV0444

Impact of the size of the pharmacodynamic Index (PDI) on risk of rmergence of bacterial resistance studied in an in-vitro model of infection

Karen E. Bowker*[1], Alan Noel[2], Marie Attwood[2], Sharon Tomaselli[2], Alasdair P. Macgowan[3]

[1]*Antimicrobial Reference Laboratory; North Bristol NHS Trust, Bristol. Uk; Severn Infection Sciences*

[2]*Bcare; Severn Infection Sciences*

[3]*North Bristol NHS Trust; Southmead Hospital ; Department of Medical Microbiology*

Background: In vitro pharmacokinetic models (IVPM) are widely used to study antibacterial drug pharmacodynamics (PD) including determining the size of the dominant PDI to reduce bacterial load but also to assess the risk of emergence of resistance (EoR). We report the results of a large series of experiments using 16 antibiotic-pathogen pairings where reduction in bacterial load and EOR were studied.

Material/methods: A single compartment dilutional IVPM was used for most experiments. Five sets of experiments were performed with MRSA, or MSSA (n=3-5 strains per experiment), six sets of experiments with *Enterobacteriaceae*, four with *P.aeruginosa*, two with *A.baumannii* and one with *Enterococcus*. Six B.lactam and seven other antibacterials were used. The size of the PDI were assessed at 24h and effect on bacterial load by changes in viable count (log CFU/ml) and EoR by changes in population profiles.

Results: Against *S.aureus* (MRSA and MSSA) the size of the PDI (AUC/MIC or T>MIC), depending on antibacterial, for a one log reduction in bacterial load was usually just larger than the AUC/MIC or T>MIC required for maximal amplification of the resistant bacterial population. Similar observations

were made with three B.lactams and an aminoglycoside tested against *Enterobacteriaceae* and also for three drugs tested against *P.aeruginosa*, *A.baumannii* and *Enterococci*.

Conclusions: Analysis of this large pre-clinical PD database of multiple drug-pathogen combination indicates that size of the PDI is related to reduction in pathogen load and EoR. The size of the PDI which is most related to EoR is just smaller than that required to cause a -1 log in bacterial load. Translation application to clinical break point setting would imply that strains with MICs on, or just below, PD breakpoints are those where EoR is most likely.