S103

1-hour Symposium

Can PK/PD get us better outcomes for infected ICU patients?

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Critically ill patients commonly develop severe infections which can have mortality rates from 20-80% in some cases. Challenges are common for clinicians in improving outcomes for these patients. Despite the presence of susceptible pathogens, patients commonly fail treatment and this in turn can manifest as patient morbidity and/or mortality or the emergence of multi-drug resistant pathogens. Whilst much investment has correctly focused on improving antimicrobial stewardship for these patients, an often overlooked aspect of treatment, is dose optimisation based on pharmacokinetic (PK)/pharmacodynamic (PD) principles. In a recent large scale observational study, The DALI Study (>400 patients in 68 intensive care units in 10 countries) it was shown that up to 20% of critically ill patients did not achieve low PK/PD targets for beta-lactam antibiotics and 50% of patients did not achieve the high PK/PD targets. When the low PK/PD targets for beta-lactam antibiotics were not achieved, these patients were three-times more likely to fail therapy and often this was associated with pathophysiological changes in PK for those patients. An understanding of changes in organ function can assist determine whether high initial doses are required for changes in the volume of distribution of drug or whether changes in the ongoing dose is required for the maintenance dose. Indeed, augmented renal clearance (ARC) is being increasingly described in subsets of critically ill patients and does result in low drug concentrations. Clinicians that identify changes in patient organ function can adjust dosing for the patient to ensure optimal drug exposures are still achieved. Therapeutic dry monitoring remains the best approach to ensure all patients achieve PK/PD targets, but this needs to be combined with accurate microbiology susceptibility reporting. Other unit-wide approaches have been attempted with varying degrees of success. In conclusion, it is clear that not achieving PK/PD targets is associated with worse patient outcomes, however, dose optimisation has not been well tested for clinical effect and we await a randomised controlled trial on this topic to quantify any benefits for critically ill patients.