



## Optimising Antibiotics and Antimicrobial Stewardship in the ICU



Antibiotic dosing regimens for critically ill patients require constant vigilance, due to extreme shifts on organ function that can impact on drug exposure. In a recent article in *Medicina Intensiva* Australian researchers Menino Cotta, Jason Roberts and [Jeffrey Lipman](#) recommend therapeutic drug monitoring and individualising and tailoring dose for antibiotics in the intensive care unit (ICU).

They explain the variations in pharmacokinetics that commonly occur among critically ill patients through existing pathophysiology as well as associated interventions. They explain initial pathophysiology of severe sepsis/ septic shock and its impact on antibiotic pharmacokinetics. The next step is to apply this knowledge when formulating dosing strategies for antibiotics based on their pathogen-exposure relationship, also known as the pharmacokinetic/pharmacodynamic (PK/PD) index.

They go on to describe how antibiotic therapy can be tailored in order to optimise desired pharmacodynamic effects. They appraise time-dependent antibiotics, concentration-dependent with time-dependence antibiotics, antibiotic dosing in multi-organ dysfunction syndrome (MODS), antibiotic dosing in continuous renal replacement therapy (CRRT) and antibiotic dosing in extracorporeal membrane oxygenation (ECMO).

Optimising antibiotic therapy needs to start with knowledge of the pharmacokinetic/pharmacodynamics of the antibiotic and take into account different treatment modalities that can influence the success of therapy, they advise.

See Also: [Antibiotic Management in the ICU](#)

### Antimicrobial Stewardship

The evidence on [effectiveness of antimicrobial stewardship \(ASP\) strategies is reviewed in an article](#) published in *Swiss Medical Weekly* in December 2015. [Dominik Mertz](#), Assistant Professor, McMaster University, Department of Medicine, Division of Infectious Diseases, and colleagues summarised and assessed the quality of evidence supporting various ASP strategies in the ICU setting, published between 2010 and 2015. The strategies assessed are 1) audit and feedback; 2) formulary restrictions; 3) guidelines/clinical pathways and mixed interventions including education and computerised decision support, and 4) procalcitonin.

The authors conclude: "While the impact of ASP intervention on appropriateness of antibiotics, utilisation and costs is fairly consistent across the studies, there is currently no convincing evidence that there is an effect on patient-important outcomes or resistance rates."

There is good evidence suggesting that audit and feedback has a positive impact on antibiotic use in ICUs

setting, and the [2007 Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship by the Infectious Diseases Society of America \(IDSA\) and the Society for Healthcare Epidemiology of America](#) rate prospective audit and feedback with an A-I grading. However, they note that due to the lack of evidence from randomised controlled trials (RCTs) the intervention rates low when using [GRADE terminology](#). In general, lack of strong evidence does not mean that ASP strategies in ICUs are not beneficial to patient outcomes, but they may be hard to detect due to small event rates of failures and the length of time until effects may affect future patients, they note.

There are a small number of recent studies on formulary restrictions and preauthorisation, which are listed as an A-II recommendation in the IDSA guidelines. The authors suggest that this might be due to the common concern of a “squeezing the balloon” phenomenon: restriction of certain classes of antibiotics may result in a reduction in use and resistance rates, but may also result in higher usage of other antibiotics. Recent studies suggest benefits from restricting and preauthorisation, but did not assess downstream effects due to increased use of other antibiotics. Again there is a low level of evidence for these strategies due to the lack of RCTs. Procalcitonin costs remain a concern.

The authors conclude: “There is no convincing evidence to support the main goal of ASP, namely to improve patient outcomes. Larger, rigorous long-term studies using a cluster randomised controlled trial or at least a controlled quasi-experimental design with time series are required to assess the impact of ASP on patient-important outcomes and on the emergence of resistance in the intensive care unit setting.”

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