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INTRODUCTION

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Nosocomial pneumonia is recognised as a persistent problem in the care of critically ill patients. It is the second most common hospital- or healthcare-associated pneumonia [1], with an incidence ranging 4–50 cases per 1,000 admissions in community hospitals and general medical wards [2], and 120–220 cases per 1,000 admissions in some intensive care units (ICUs) [3]. Clinical and diagnostic approaches for the management of nosocomial pneumonia have been developed that make the best use of available antimicrobial treatments and minimise the increase in microbial resistance rates, a rising challenge to effective management.

As a resource for the practicing clinician, the American Thoracic Society and the Infectious Diseases Society of America have updated their guidelines for treating nosocomial pneumonia [4]. Additionally, at the 16th Annual Congress (Munich, Germany) of the European Respiratory Society, a symposium sponsored by Janssen–Cilag titled ''Best use of antibiotics in nosocomial pneumonia: improving efficacy and limiting resistance'' was held to further inform clinicians on the optimisation of antibiotic therapy for nosocomial pneumonia. The emphases were on the role of appropriate initial therapy, de-escalation, short-duration therapy and the optimisation of therapy using pharmacokinetic (PK) and pharmacodynamic (PD) principles. Optimised antibiotic therapy holds great promise for improving patient outcomes and decreasing the emergence of resistance. Each of the articles in the present review is based on the author's presentation and respective expertise in optimising antibiotic therapy.

RELLO [5], Chief of the Critical Care Department at the Joan XXIII University Hospital in Tarragona, Spain, reviewed the importance of appropriate initial antibiotic therapy and de-escalation. As multidrug resistance increases in the ICU in patients treated for nosocomial pneumonia, costs, morbidity and mortality rise. The inappropriate choice of antibiotics is the most important independent risk factor for death. Traditionally, a narrow-spectrum drug was used first, with the more potent broad-spectrum drugs reserved for subsequent use. Currently, however, a new approach starts with a high-dose, broad-spectrum antibiotic and then, based on microbiological results, tailors the individual therapy. Carbapenems and the cephalosporin cefepime have great efficacy against both extended-spectrum β-lactamase- and AmpC-producing pathogens. Doripenem, an investigational carbapenem that has completed phase III clinical trials, has shown enhanced activity against *Pseudomonas aeruginosa* and a low potential for seizures both *in vitro* and in animal models. It has broad-spectrum efficacy against both Gram-positive and Gram-negative pathogens (with a low propensity for resistance) and may help reduce the costs, morbidity and mortality of nosocomial pneumonia.

CHASTRE [6], Professor of Medicine at the Université Pierre et Marie Curie in Paris, France, focused on optimising the duration of antibiotic therapy for ventilator-associated pneumonia (VAP). ICUs face the emergence and rapid dissemination of multidrug-resistant bacteria, especially *P. aeruginosa* and Acinetobacter spp. The traditional approach was to treat nosocomial infections for 14–21 days at the cost of increased toxicity, added expense and the emergence of multidrug-resistant bacterial strains. A prospective randomised trial of an antibiotic discontinuation policy for clinically suspected VAP found that a decrease in the overall duration of antibiotic treatment could be safely achieved without increasing secondary episodes of VAP, hospital mortality or length of stay in the ICU. Therefore, if patients receive an initial appropriate antibiotic regimen for VAP, a shortened 7-day therapy may produce an effective response and clinical resolution of the infection.

DRUSANO [7], Co-Director of the Ordway Research Institute in Albany, NY, USA, reviewed how the combined PK and PD profiles of a β-lactam can be used to cure the greatest percentage of patients by achieving the PD target associated with a favourable outcome, while minimising the development of resistant organisms. A Monte Carlo simulation generates an empirical, rational dose selection and strategy against the targeted pathogen's minimum inhibitory concentration (MIC). For a carbapenem, the exposure target is for free drug levels to be >MIC for 40% of the dosing interval. By extending the infusion period, a lower dose can achieve almost the same efficacy as a higher dose infused over a shorter period of time, in addition to reducing cost, toxicity and the likelihood for the emergence of resistance.

Finally, I, as Chairman of the symposium, discussed the use of monotherapy *versus* combination therapy for nosocomial pneumonia [8].

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The emerging antibiotic resistance in the ICU is driving doctors to optimise antibiotic therapy by using a combination of antibiotics, although clinical data in support of this are lacking. Combination therapy is thought to have a broader antimicrobial spectrum, synergism and decreased emergence of resistance, with reduced associated costs and toxicity. The main strategy for treating any suspected nosocomial pneumonia, whether *via* combination therapy or monotherapy, should be early, appropriate and adequate, based on multidrug-resistant risk factors and local resistance patterns. De-escalation should be based on both clinical response and microbiological results. If pneumonia is confirmed, the duration of therapy should be limited to 7–8 days; if not, antibiotics should be stopped.

In summary, the current group of experts agreed that the cardinal principles of clinical management of nosocomial pneumonia are: 1) to provide early, appropriate and adequate therapy based on risk factors for multidrug-resistant pathogens and local risk factors; 2) to assess the response and de-escalate therapy based on both clinical response and cultures as well as Gram stains (antibiotics should be stopped if there is no evidence of pneumonia); 3) to use extended infusions of β-lactams to increase efficacy, minimise the emergence of resistance and decrease cost and toxicity; 4) to avoid extended (>7–8 days) antibiotic therapy in patients who respond; and 5) to emphasise prevention with zero tolerance for avoidable risk factors.

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