

Antibiotic stewardship in the intensive care unit: tools for de-escalation from the American Thoracic Society Meeting 2016

Kevan Akrami^{1,2}, Daniel A. Sweeney³, Atul Malhotra³

¹Department of Infectious Disease, University of California, San Diego, USA; ²Critical Care Medicine, National Institute of Health, Bethesda, MD, USA; ³Department of Pulmonary, Critical Care and Sleep Medicine, University of California, San Diego, USA

Correspondence to: Atul Malhotra, MD. Division of Pulmonary, Critical Care and Sleep, University of California, San Diego, USA. Email: amalhotra@ucsd.edu.

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There was considerable discussion about the importance of antibiotic stewardship at the American Thoracic Society meeting in San Francisco in May 2016. Extensive literature in critical care suggests that use of early empiric antibiotics for the treatment of suspected sepsis and septic shock is crucial to clinical outcomes with delays in therapy being associated with increased mortality (1,2). As a result, much effort has been placed on facilitating the timely administration of antibiotics for patients who are septic or at risk of sepsis. However, both the emergence of resistant pathogens and antibiotic-related complications has led to discussion regarding appropriate antibiotic management. While there is clear evidence that early initiation of antibiotics in patients at risk of sepsis impacts mortality, the de-escalation and discontinuation of antibiotics is also important in the management of the critically ill. Several concepts emerged from the ATS sessions and from the recent literature:

(I) A general principle of “start broadly, narrow quickly, if they don’t need it get rid of it” has been proposed for antibiotic management in sepsis. The concept underlying is that withholding antibiotics is deleterious for patients with sepsis and proven infection. Conversely, continuing broad spectrum antibiotics inappropriately leads to emergence of resistant pathogens which has implications both for the individual patient and the broader intensive care unit (ICU) population. Thus, narrowing antibiotics based on culture results is recommended and can help to minimize the complications related to antibiotics. However, in patients where infection is either ruled out or resolved, the discontinuation of

antibiotics occurs infrequently resulting in significant consequences for the general ICU population and the individual patient;

- (II) Complications of antibiotics are worth considering. For an individual, antibiotic complications might include the selection of resistant pathogens which become difficult to treat if secondary infection occurs. Moreover, antibiotics can contribute to the development of *C. difficile* infection, fungal infection, cytopenias, acute renal failure and other complications. In addition, antibiotic therapy for an incorrect diagnosis may obscure the actual diagnosis which could delay definitive therapy. For example, a patient who is receiving therapy for misdiagnosed ventilator-associated pneumonia might have a poor clinical outcome if the true cause of sepsis were empyema, cholecystitis or some other diagnosis. Non-infectious mimics of sepsis also may be overlooked in the setting of a misdiagnosis. Thus, individual patients may be inadequately treated for infection without appropriate consideration of alternative diagnoses. Given that duration of ICU stay is associated with poor prognosis, one famous ICU proverb is “if you are treated in the ICU with the wrong diagnosis, you will die in the ICU with the wrong diagnosis.” Furthermore, the broader ICU population may suffer from inappropriate antibiotic therapy to an individual as evidenced by temporary ICU closures due to emergence of highly drug resistant pathogens;
- (III) The lack of guidelines to aid in the de-escalation of antibiotics and the paucity of rigorous clinical trials of markers to assist in de-escalation presents

a significant barrier to antibiotic stewardship in the ICU. Rapid diagnostic tests may hold the key to the development of rational strategies for antimicrobial stewardship in the ICU. The use of procalcitonin levels was discussed as a method to guide antibiotic therapy (3). Procalcitonin is elevated in bacterial infection. And while starting or withholding antibiotics based on a procalcitonin level may not be feasible, serial measures may potentially be used as a guide to de-escalate antibiotic therapy (4). In addition, polymerase chain reaction (PCR) and mass spectrometry technology continues to expand such that specific infectious organisms can be identified more rapidly than by traditional culture technique. PCR-based testing, always in conjunction with clinical judgement, can be used to decide whether to treat for influenza or *C. difficile* infection. Likewise, the nasal swab MRSA PCR assay has been studied as a tool to predict whether a patient is at risk for MRSA pneumonia (5). Besides PCR based assays, antimicrobial stewardship teams armed with matrix assisted laser desorption/ionization time-of-flight (MALDI-TOF) data were able to decrease the time needed to identify a specific infectious organism, resulting in a shorter time to effective antibiotic therapy (6). Multiplex molecular assays have also been used to provide a rapid microbiological diagnosis of bacterial and non-bacterial infections compared with routine culture approach (7,8). In addition, identification of the presence or absence of genes conferring resistance will aid in earlier appropriate antibiotics and subsequent de-escalation (9). Such approaches could be helpful in guiding therapy to avoid unnecessary antibiotics and provide narrow spectrum treatment in the appropriate setting (9-11).

In conclusion, various guidelines and quality initiatives have emphasized the proven benefits of prompt antibiotic therapy for septic patients. Unfortunately the process of de-escalating antibiotic regimens in such a manner that is both safe and beneficial to the recovering septic patient has not been well studied. Besides the need for more rigorous data to support the use of rapid diagnostics, other factors may be equally important in developing antibiotic de-escalation strategies including: the formation of multidisciplinary antimicrobial stewardship teams (pharmacy, infectious disease and critical care specialists); the development of ICU dedicated antibiograms; and the use of electronic medical record decision support software (12). As the impact of

these initiatives is evaluated in the coming years, critical care physicians will be tasked with leading the movement towards rational, evidence-based de-escalation strategies starting in the ICU.

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Footnote

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