Interprofessional Approaches to Promote Stewardship in the ICU

Online Newsletter

Target Audience

This continuing medical education activity meets the needs of pulmonologists, critical care specialists, and other healthcare professionals involved in the management of HABP/VABP.

Learning Objectives

Upon completing this activity, participants will be able to:

- Identify management approaches that adhere to antimicrobial stewardship principles when managing critically ill patients with acute respiratory tract infections caused by MDR Gram-negative bacteria
- Explain the role of interdisciplinary collaboration within the critical care setting in optimizing patient outcomes when managing patients with HABP/VABP

Expert Faculty

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Accreditation

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Disclosures

Scott T. Micek, PharmD has relevant financial relationships with the following commercial interests:
Advisory Board: Paratek Pharmaceuticals
Research Support: Paratek Pharmaceuticals
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Editor's Note

In any healthcare setting, the success of an antimicrobial stewardship program (ASP) will depend on interprofessional communication and collaboration. This collaboration is even more important when managing critically ill HABP/VABP patients in the ICU setting where there is little room for error and initial inappropriate therapy will have dire consequences. Antimicrobial stewardship teams (ASTs) must work together to identify areas within their institution that need improvement, design and implement strategies that adhere to stewardship principles, and measure outcomes to demonstrate any benefits of these strategies. Key members of ASTs include the Infectious Disease physician and an ID-trained pharmacist, but should also involve a wide variety of healthcare professionals that can include microbiologists, epidemiologists, nurses, Infection Control, and Information Technologists, among others.

We recently had a discussion with Dr. Scott Micek, PharmD, Professor of Pharmacy Practice and Director of the Center for Health Outcomes, Research and Education at St. Louis College of Pharmacy, regarding the importance of interprofessional collaboration when designing and implementing antimicrobial stewardship tactics in the ICU setting. Dr. Micek reviewed two antimicrobial stewardship strategies that are commonly utilized in patients with HABP/VABP that aim to reduce antimicrobial-resistance development and healthcare utilization without negatively impacting clinical outcomes.

Duration of Therapy

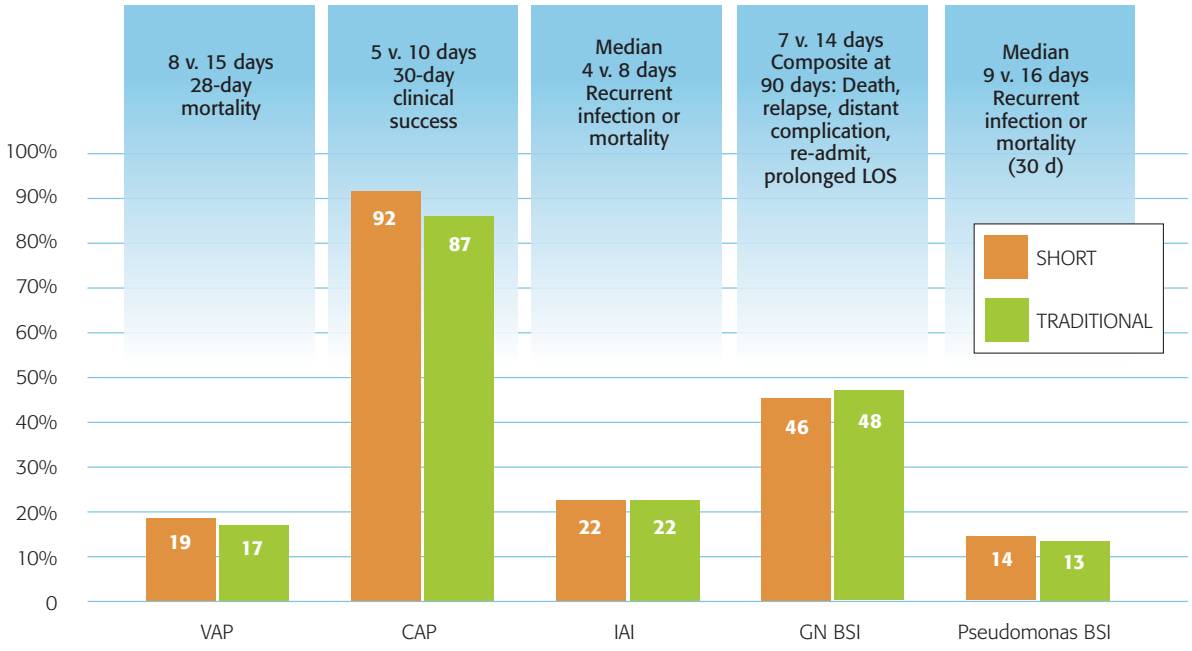
Q: *Does a shorter duration of antimicrobial therapy result in negative clinical outcomes?*

One of the first studies I did with Dr. Marin Kollef at Barnes Jewish Hospital in St. Louis, MO was to compare early discontinuation of antibiotic therapy in VAP patients and I was involved in the interventional arm. In the study, patients were randomized to have their duration of therapy determined by either an antibiotic discontinuation team (discontinuation group) or by their treating physician team (conventional group) (Micek 2004). Certain parameters had to be met for early discontinuation, namely resolution of signs and symptoms of active infection that can include absence of fever (temperature <38.3°C), WBC <10,000/mm^3 or a drop of 25% from its peak, chest radiograph revealing improvement or no progression, absence of purulent sputum, and PaO_2:FiO_2 >250. In the discontinuation cohort, a pharmacist or pharmacist group recommended to the nursing or physician group for discontinuation if the clinical criteria were met. The result of the study showed that patients in the discontinuation group had a significant reduction in the duration of antibiotic therapy, dropping from about 8 days in the conventional group to 6 days in the discontinuation group (p=0.001). Interestingly, we saw no adverse outcomes with shorter duration of therapy in these patients, such as mortality, length of stay, or subsequent infection.

Outcomes	Discontinuation Group (n=150)	Conventional Group (n=140)	P value
Days of antibiotic therapy	6.0 ± 4.9	8.0 ± 5.6	0.001
Hospital mortality	48 (32.0)	52 (37.1)	0.357
Hospital LOS, days	15.7 ± 18.2	15.4 ± 15.9	0.865
ICU LOS, days	6.8 ± 6.1	7.0 ± 7.3	0.798
Duration of ventilation, days	5.4 ± 5.7	5.7 ± 7.1	0.649
Subsequent infection	56 (37.3)	46 (32.9)	0.425

Source: Micek 2004

In the general landscape these days, the belief is that shorter durations of antimicrobial therapy are acceptable. The figure below summarizes a variety of studies that compared shorter versus longer durations of antimicrobial therapy for different types of infections. The results show that cutting the duration of therapy by about a half resulted in no significant impact on outcomes. For example, in the Chastre, et al study that included patients with VAP, antimicrobial treatment for either 8 days or 15 days resulted in similar rates of 28-day mortality (Chastre 2003). Another study the looked at pseudomonal bloodstream infections revealed that shortening the duration of therapy from 16 days to only 9 days did not impact the rate of recurrent infection or 30-day mortality (Fabre 2019).



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Q: *Does a shorter duration of therapy reduce resistance development?*

Longer duration of therapy can result in collateral damage. In another study published together with my colleagues, we looked at patients with severe sepsis or septic shock, of which the majority had HAP or VAP as the source of infection (Teshome 2019). If you evaluate their cumulative exposure to antibiotics, we found that each additional day of exposure can predispose patients to subsequent risk for resistance development. The table below shows the adjusted hazard ratio of each day of exposure to various antimicrobials, and if we look at the risk of exposure to any antibiotic, there is a substantial and significant risk for resistance with prolonged therapy. For example, when considering the use of cefepime, a 10-day course of antibiotics is associated with a 24% increased risk of resistance development when compared to a 7-day course. So, based on these results, prolonged durations of antibiotics can lead to an increase in risk of resistance development.

	Cefepime (n=5274)	Meropenem (n=3625)	Pip-tazo (n=2463)	Any antibiotic (n=7118)
	Adjusted hazard ratio (95% CI)			
Each additional day of exposure	1.08 (1.07–.09)	1.02 (1.01–1.03)	1.08 (1.06–1.09)	1.04 (1.04–1.05)

Source: Teshome 2019

To further support the finding that each additional day of antimicrobial therapy increases the risk of resistance development, a retrospective observational study was performed by Ramen et al. where they evaluated antimicrobial utilization and outcomes in VAP patients who had a culture-negative quantitative bronchoscopy and whose antibiotic discontinuation was either early or late (Ramen 2013). Median antibiotic duration was 4 days in the early discontinuation group versus 9 days in the late discontinuation group. Though there was no significant difference in hospital mortality between the two groups, those who had early discontinuation of antibiotic therapy had a significantly lower rate of superinfection (p=0.008) and multidrug-resistant superinfections (p=0.003). Thus, even in critically ill patients, reducing the duration of antimicrobial therapy under certain circumstances will not adversely impact clinical outcomes but can be beneficial in reducing the risk of resistant infections. It is important to keep in mind that the decision to discontinue therapy should be the result of an interprofessional discussion and based on patient clinical resolution of symptoms and risk factors.

Variable	Early discontinuation (n=40)	Late discontinuation (n=49)	P value
Antibiotic days, median (IQR)	4 (3, 4)	9 (6, 14)	<0.001
Hospital mortality	25%	30%	0.642
Superinfection	22.5%	42.9%	0.008
MDR superinfection	7.5%	35.7%	0.003

Source: Ramen 2013

De-escalation of Therapy

Q: *What is the role of de-escalation of therapy in the ICU?*

De-escalation of antimicrobial therapy is another important strategy to minimize the risk of resistance development without adversely affecting clinical outcomes. Individuals with or suspected of HABP/VABP typically receive broad-spectrum antimicrobial therapy that can cover both Gram-positive and Gram-negative pathogens. Initial antimicrobial selection should be based on patient risk factors for resistant pathogens and local epidemiology, preferably with a unit-based antibiogram. Once the causative organism and its susceptibility profile are determined, current guidelines recommend de-escalation of therapy from the empiric broad-spectrum regimen to a narrower antibiotic regimen, typically by switching from combination therapy to monotherapy if appropriate. However, in clinical practice, de-escalation is not always performed. In a survey of clinicians attending the live CME symposium, when asked if de-escalation of therapy is a priority at their institution, nearly one-third reported that it is only somewhat of a priority and not performed as often as it should for their patients.

Q: *What is the evidence that de-escalation of therapy can improve outcomes?*

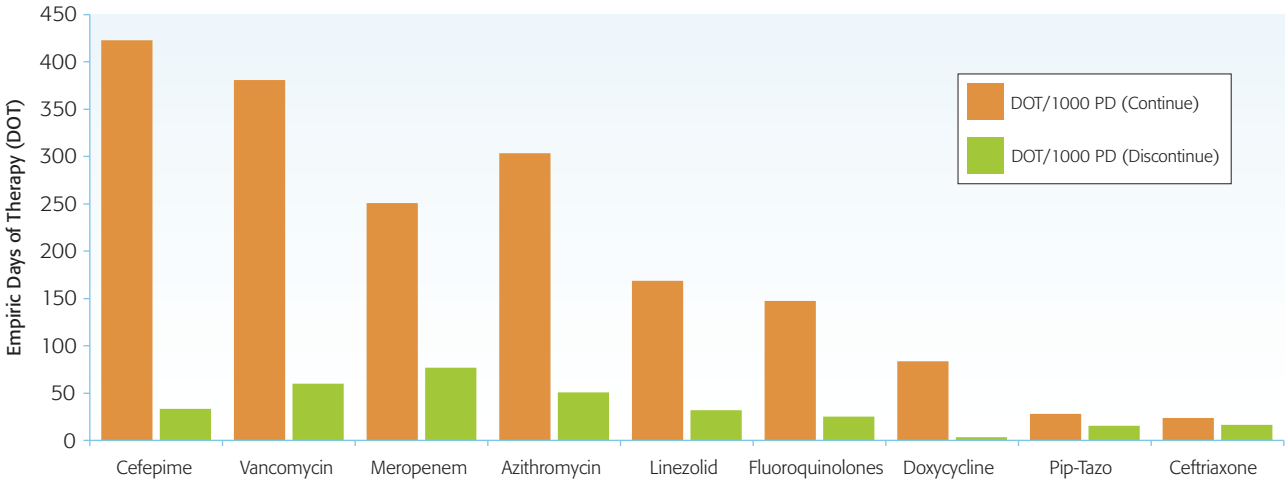
In a single-center retrospective cohort study that was recently published with my colleagues, we looked at the impact of de-escalation of anti-MRSA agents in nosocomial pneumonia patients who had a negative respiratory culture (Cowley 2019). Patients in the de-escalation group predominantly had discontinuation of vancomycin if MRSA was not identified in respiratory cultures. What we saw from the results was that, despite decreasing the median duration of anti-MRSA therapy from 8 days to 3 days, there was no significant impact on 28-day mortality. However, there was a beneficial impact in reducing hospital LOS as well as decreasing the rate of acute kidney injury with de-escalation of therapy.

Variable	De-escalation (n=92)	No De-escalation (n=187)	Difference (95% CI)
Duration of treatment, median (IQR), days	3 (2-4)	8 (7-11)	5 (5 to 6)
28-day mortality	23%	28%	-5.5 (-16.1 to 6.5)
Hospital LOS after index date, median (IQR), days	15 (8-30)	20 (11-34)	3.2 (0.1 to 6.4)
New acute kidney injury	36%	50%	-13.8 (-26.9 to -0.4)

Source: Cowley 2019

Q: *How can new technologies be used to expand opportunities for stewardship?*

In addition to culture and susceptibility results, the use of rapid diagnostic techniques can aid clinicians in promoting stewardship principles in the clinical setting. In another retrospective cohort study that we published a few years ago, we evaluated the impact of continuing antibacterial therapy in cases of viral pneumonia, looking at the clinical outcomes and subsequent MDR infection. For these patients, a rapid diagnostic approach that included a respiratory viral panel was used to determine the potential cause of pneumonia. When a viral pathogen was identified, we entrusted that this could be the cause of infection and would thus discontinue the use of antibacterial therapy. The figure below shows the number of days of therapy for the various antimicrobials used for patients who continued on therapy compared to those who discontinued therapy based on the rapid diagnostic assay. When we compared subsequent MDR infection or colonization between the two groups, it was found that 53% of those who continued antibiotic therapy had a subsequent MDR infection or colonization compared to only 21% of those who discontinued therapy (p=0.027). The main point from this study, as was discussed previously, is that if you continue with antibiotics, you are predisposing your patients to subsequent infection with a multidrug-resistant organism.



Source: Crotty 2015

Closing Thoughts

Antimicrobial stewardship strategies aim to improve patient outcomes while reducing the risk for resistance development. Key to the success of these programs relies on interprofessional collaboration to identify practice needs and gaps at an institution followed by design and implementation of an appropriate intervention. Here, we describe two strategies, shortening duration of therapy and de-escalation of therapy, that aim to reduce antimicrobial use without adversely impacting patient outcomes. Yet, the evidence consistently demonstrates a reduction in the risk of MDR infection with decreased antimicrobial exposure. Despite the potential benefits of limiting antimicrobial exposure, the decision to discontinue or de-escalate therapy should be based on a number of patient factors as well as a team-based discussion. This is particularly important when managing critically ill patients to ensure the best possible outcome.

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