Antimicrobial Stewardship News
Volume 4, Number 8
August 2016

dason | DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

Review of the 2016 IDSA/ATS Practice Guidelines for the Management of Adults with Hospital-acquired (HAP) and Ventilator-associated Pneumonia (VAP)

Background

Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) continue to be frequent complications of hospital care with negative impacts on patient outcomes.[1] The Infectious Diseases Society of America (IDSA) and American Thoracic Society (ATS) recently published updated guidelines designed to provide guidance on the diagnosis and management of nonimmunocompromised patients with HAP/VAP and serve as the basis for development and implementation of locally adapted guidelines. There are several major changes to the guidelines, including: (1) removal of the concept of Health Care Associated Pneumonia (HCAP); (2) emphasis on local antibiograms to guide empiric antibiotic selection; (3) new indications for empiric dual Gram-negative and methicillin-resistant *Staphylococcus aureus* (MRSA) therapy; and (4) recommendation for short-course antibiotic therapy for most patients with HAP or VAP independent of microbial etiology. The goal of this newsletter is to highlight the components of the guidelines that are most useful for stewardship programs in DASON hospitals.

Removal of HCAP from Guidelines

In the 2005 update, there was emphasis and differentiated management for patients with Health Care Associate Pneumonia (HCAP). This definition tried to address the increased risk of resistant infections seen in some patients; however, there is increasing evidence that many patients defined as having HCAP are not at high risk for multidrug-resistant (MDR) pathogens.[2-7] Therefore, recommendations for this population of patients (with significant healthcare exposure) will be included in the upcoming community-acquired pneumonia (CAP) guidelines expected to be released in Summer 2017. The focus of the current guideline update is the management of non-immunocompromised patients with HAP/VAP, which are defined as follows:

- Hospital-acquired pneumonia (HAP): pneumonia that occurs 48 hours or more after admission, which was not incubating at the time of admission.[2]
- Ventilator-associated pneumonia (VAP): pneumonia that arises more than 48-72 hours after endotracheal intubation.[2]

> **Health Care Associated Pneumonia (HCAP) not included in guideline update**

"Targeted" Empiric Treatment Regimens

The current guidelines emphasize selecting empiric treatment regimens based on local distributions of pathogens and their antimicrobial susceptibilities. It is recommended that all hospitals regularly generate and distribute a local antibiogram, ideally one that is specific to their intensive care population. The goal is to target specific pathogens associated with HAP/VAP as narrowly as possible to assure adequate treatment, while minimizing overtreatment and undesirable consequences. In addition to local antibiograms, patient-specific risk factors (**Table 1**) are used to identify patients at risk for MDR pathogens who may require broader coverage.

> **Local antibiograms should be used to guide selection empiric treatment regimens**

Empiric Treatment for HAP/VAP

In patients with no risk factors for MDR pathogens (**Table 1**), empiric therapy should include an agent with activity against *Pseudomonas aeruginosa* and other Gram-negatives as well as methicillin-sensitive *S. aureus* (MSSA). Regimens including piperacillin-tazobactam, cefepime, levofloxacin, imipenem-cilastatin, or meropenem are suggested. Selection of the primary agent should be based upon local antibiograms. Importantly, a single agent with anti-pseudomonal activity is adequate as long as local resistance rates do not exceed 10% for the selected agent. Antibiotic dosing should be determined using pharmacokinetic and pharmacodynamic data, rather than the manufacturer's prescribing information. In general, DASON recommends avoidance of carbapenems and fluoroquinolones as first-line therapy in patients without MDR risk factors because 1) carbapenems should be reserved for patients with risks for MDR, and 2) fluoroquinolones carry additional risks of unintended consequences (e.g. *C. difficile*) and resistance rates in most hospitals are >10% for common Gram-negative pathogens (e.g. *E. coli*).

When to cover MRSA

Agents targeting MRSA (vancomycin or linezolid) are recommended for empiric use in HAP/VAP patients with a risk factor MRSA infection (**Table 1**), patients in units where >10-20% of *S. aureus* isolates are methicillin-resistant, and patients in units where the prevalence of MRSA is not known. The risk factor most associated with MRSA risk is prior receipt of intravenous antibiotics in the past 90 days. Patients requiring ventilator support due to pneumonia or septic shock should be covered for MRSA. There is no preference for the use of linezolid over vancomycin.

When to Double-cover *Pseudomonas*

Two agents from different classes are recommended for empiric therapy in patients with a risk factor for MDR Gram-negative pathogens (**Table 1**), patients in units where >10% of Gram-negative isolates are resistant to an agent being considered for monotherapy, and patients in

an ICU where local antimicrobial susceptibility rates are not available. In addition, all patients with bronchiectasis or cystic fibrosis should receive two empiric antipseudomonal agents. Patients requiring ventilatory support due to pneumonia or septic shock should also receive dual-antipseudomonal coverage.

A weak recommendation is provided to avoid aminoglycosides and colistin for empiric therapy if other options with adequate Gram-negative activity are available to limit toxicities. The guidelines also comment that it is acceptable to use aztreonam as a second agent with another beta-lactam when options are limited based on a rationale that the bacterial cell wall target for aztreonam is different from other beta-lactams. However, if aztreonam is selected the other agent must include adequate coverage of *S. aureus*.

Table 1. Risk factors for multidrug-resistant pathogens

Ventilator-associated Pneumonia (VAP)	Hospital-acquired Pneumonia (HAP)
MDR pathogens • Prior IV antibiotic use within 90 days • Septic shock at time of VAP • ARDS preceding VAP • $\geq$ 5 days of hospitalization prior to VAP onset • Acute renal replacement therapy prior to VAP onset	MDR pathogens • Prior IV antibiotic use within 90 days
MRSA • Prior IV antibiotic use within 90 days	MRSA • Prior IV antibiotic use within 90 days • Need for ventilatory support or septic shock
MDR *Pseudomonas* • Prior IV antibiotic use within 90 days • Bronchiectasis or cystic fibrosis	MDR *Pseudomonas* • Prior IV antibiotic use within 90 days • Bronchiectasis or cystic fibrosis • Need for ventilatory support or septic shock

_____

Antibiotic De-escalation

In patients with HAP/VAP who are not at risk for MDR infections, have a negative sputum culture, and are clinically improving, clinicians should empirically de-escalate antibiotic therapy. In most cases, this means that anti-pseudomonal coverage should be dropped. A single broad-spectrum antibiotic should be selected according to a local antibiogram, or, if not available, with adequate activity against enteric Gram-negatives and MSSA. Patients with poor-quality or no sputum cultures and patients at high risk for MDR infections may not be appropriate candidates for empiric de-escalation. In patients with positive sputum cultures, therapy should be tailored based on the results of antibiotic susceptibility testing. In clinically stable patients with *P. aeruginosa* pneumonia, it is not necessary to continue double coverage.

Many facilities are using procalcitonin to guide antibiotic decisions in sepsis. In addition to this indication, procalcitonin levels may be used in combination with clinical criteria to guide the discontinuation of antibiotic therapy in patients with HAP/VAP.

Duration of Therapy

In most patients with HAP/VAP, regardless of microbial etiology, the duration of antibiotic therapy should be 7 days. This recommendation was based on two meta-analyses suggesting there was no difference between short-course (i.e., 7-8 days) and long-course antibiotic regimens (i.e., 10-15 days) in regards to mortality, treatment failure, recurrent pneumonia, or duration of mechanical ventilation.[8,9] This is a change from the old guideline, which suggested that certain pathogens (e.g. non-lactose fermenting Gram-negatives) should be treated with longer durations due to risk of recurrence. This recurrence risk was not observed in the more recent data cited above and thus the practice guideline was adjusted. There are exceptional situations where longer courses may still be appropriate due to delayed clinical response.

> **Many patients will qualify for antibiotic de-escalation!**

Guideline Implementation Strategies

Both passive and active stewardship interventions can be implemented based on the IDSA/ATS HAP/VAP guidelines. Passive stewardship interventions, including educating providers, updating and distributing local antibiograms, and creating or modifying existing local treatment protocols or ordersets are inexpensive and effective ways to improve antibiotic utilization, guideline concordance, and patient care. Specifically, education topics may include appropriate duration of therapy, indications for dual-antipseudomonal and MRSA coverage, and opportunities for antibiotic de-escalation. These efforts should be directed towards providers in intensive care units and wards. In addition, displaying guideline recommendations in highly visible areas for medical providers, including inpatient workrooms, may augment this intervention. Active antimicrobial stewardship strategies, including performing antibiotic time-outs or audit and feedback, can be implemented once problematic areas are identified on broad-spectrum antibiotic audits and reports.

Take Home Points

1. HCAP is no longer included in the HAP/VAP guidelines.
2. Empiric treatment for patients without risks for MDR should cover *P. aeruginosa* and MSSA and be based on local antibiograms.
3. Decisions to cover MRSA or double-cover Gram-negatives should be guided by the patient's clinical stability, risks for MDR, and local antibiograms.
4. De-escalation should be actively practiced, especially in clinically responsive patients with negative cultures.
5. The duration of antibiotic therapy should be limited to 7 days in most cases.

dason | DUKE ANTIMICROBIAL STEWARDSHIP OUTREACH NETWORK

References

1. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis.* 2016.
2. American Thoracic S, Infectious Diseases Society of A. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med.* 2005;171(4):388-416.
3. Chalmers JD, Rother C, Salih W, Ewig S. Healthcare-associated pneumonia does not accurately identify potentially resistant pathogens: a systematic review and meta-analysis. *Clin Infect Dis.* 2014;58(3):330-339.
4. Gross AE, Van Schooneveld TC, Olsen KM, et al. Epidemiology and predictors of multidrug-resistant community-acquired and health care-associated pneumonia. *Antimicrob Agents Chemother.* 2014;58(9):5262-5268.
5. Yap V, Datta D, Metersky ML. Is the present definition of health care-associated pneumonia the best way to define risk of infection with antibiotic-resistant pathogens? *Infect Dis Clin North Am.* 2013;27(1):1-18.
6. Jones BE, Jones MM, Huttner B, et al. Trends in Antibiotic Use and Nosocomial Pathogens in Hospitalized Veterans With Pneumonia at 128 Medical Centers, 2006-2010. *Clin Infect Dis.* 2015;61(9):1403-1410.
7. Valles J, Martin-Loeches I, Torres A, et al. Epidemiology, antibiotic therapy and clinical outcomes of healthcare-associated pneumonia in critically ill patients: a Spanish cohort study. *Intensive Care Med.* 2014;40(4):572-581.
8. Pugh R, Grant C, Cooke RP, Dempsey G. Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults. *Cochrane Database Syst Rev.* 2015(8):CD007577.
9. Dimopoulos G, Poulakou G, Pneumatikos IA, Armaganidis A, Kollef MH, Matthaiou DK. Short- vs long-duration antibiotic regimens for ventilator-associated pneumonia: a systematic review and meta-analysis. *Chest.* 2013;144(6):1759-1767.

dason news

- MARK YOUR CALENDARS! The DASON Continuing Education series program titled "Incorporating Procalcitonin testing in Sepsis Protocols" will be held on August 4 and 11 via webinar. Emails for registration will be circulated soon.
- Please return your comments on the Centers for Medicare and Medicaid proposed Conditions of Participation to Libby at libby.dodds@duke.edu by Friday, August 5th.
- MARK YOUR CALENDARS! The DASON/DICON Fall 2016 Symposium will be held on Friday, November 18 at the Sheraton Greensboro Hotel at Four Seasons from 8:30AM-3:30PM – We look forward to seeing you there!