Antimicrobial Stewardship News

Volume 8, Number 7

July 2020

Part II: Dropping Empiric Vancomycin for Community-acquired Pneumonia

The 2019 update[1] to the clinical practice guidelines for treatment of Community-acquired pneumonia (CAP) removed the previous category of health care associated pneumonia (HCAP) that drives use of anti-pseudomonas and anti-MRSA therapies. These guidelines represent a significant practice change and understandably, front-line clinicians have questioned the safety of eliminating these broad-spectrum therapies from empiric regimens for hospitalized patients with CAP.

In the June 2020 DASON newsletter, a clinical prediction score, the DRIP Score was described as a mechanism to decrease empiric anti-pseudomonas therapy in CAP patients. This newsletter reviews a recent publication investigating the use of empiric vancomycin in the treatment of CAP. These data further support the current IDSA guideline recommendation of using nasal MRSA PCR to either discontinue (or delay starting) vancomycin in CAP patients.

Jones and colleagues conducted a large, retrospective review of 88,605 inpatients treated for CAP from 2008 to 2013 within the Veterans Health Administration system.[2] The principal aim was to compare 30-day mortality between patients who received empirical anti-MRSA therapy (e.g. vancomycin or linezolid) to those who received guideline-recommended standard therapy (e.g. beta-lactam with azithromycin/doxycycline or respiratory fluoroquinolone). Patients were stratified into three categories based upon initial empirical antibiotic therapy:

1. anti-MRSA therapy with standard therapy, OR
2. anti-MRSA therapy without standard therapy, OR
3. standard therapy alone

The standard therapy cohort served as a reference group. Patients were excluded from evaluation if they did not receive antibiotics within 24 hours of admission, had been hospitalized for pneumonia in the previous month, or were transferred from an outside hospital.

Table 1. Adjusted Risk Ratios with Anti-MRSA Therapy

Group	Adjusted Risk Ratio (95% CI)	
	Anti-MRSA Therapy *Plus* Standard Antibiotics	**Anti-MRSA Therapy *Without* Standard Antibiotics**
All patients	1.4 (1.3-1.5)	1.5 (1.4-1.6)
Patients admitted to ICU	1.3 (1.2-1.5)	1.4 (1.2-1.5)
High clinical risk for MRSA	1.2 (1.1-1.4)	1.3 (1.1-1.4)
MRSA surveillance PCR positive	1.6 (1.3-1.9)	1.8 (1.4-2.3)
MRSA culture positive	1.1 (0.8-1.4)	1.2 (0.9-1.6)

In order to minimize confounding by indication, the authors performed a weighted propensity score analysis determined from 41 patient characteristics. An instrumental variable analysis attempted to mitigate bias of anti-MRSA therapy prescribing to those with an unmeasurable perceived greater risk. Examined secondary outcomes included risk of acute kidney injury, new or recurrent *C. difficile* infection, and detection of VRE and gram-negative rods (GNR) in urine or blood samples.

Patients receiving MRSA-active therapy had higher rates of comorbid disease, higher Pneumonia Severity Index scores, and greater 30-day mortality in comparison to patients receiving standard therapy alone. After performing the weighted propensity analysis, empirical anti-MRSA therapy with standard therapy (adjusted risk ratio 1.4, 95% CI 1.3–1.5) or without standard therapy (aRR 1.5, 95% CI 1.4-1.6) remained associated with a greater risk of 30-day mortality (Table 1).

Incidence of MRSA in CAP:

Consistent with prior studies, 38% of included patients received therapy effective against MRSA (vancomycin or linezolid).

MRSA was detected from clinical (blood or sputum) cultures in only 2% of patients in this cohort.

This finding held in subgroup analyses which evaluated patients more likely to benefit from empiric anti-MRSA therapy, including patients requiring ICU admission, patients deemed high-risk for MRSA by guideline criteria, and patients with MRSA detected by surveillance PCR. Interestingly, no mortality difference was detected in patients with an MRSA-positive clinical culture (Table 1).

Importantly, the authors reported empiric anti-MRSA therapy increased risk of all proposed adverse outcomes—renal dysfunction (aRR 1.4, 95% CI 1.3-1.5), *C. difficile* infection (aRR 1.6, 95% CI 1.3-1.9), VRE (aRR 1.6, 95% CI 1.0-2.3) and GNR (aRR 1.5, 95% CI 1.2-1.8) infection or colonization.

The results of this large observational study challenge the widespread use of empiric vancomycin for CAP, even for those with greatest potential risk for MRSA pneumonia. However, these findings should be appropriately interpreted. While the authors attempted to minimize confounding by indication using statistical techniques, it is likely that residual bias remained. For example, it seems unrealistic that empiric vancomycin alone could have the strong, detrimental effect on 30-day mortality reported here. However, the consistency of effects demonstrated in this study certainly suggest against any benefit of empiric vancomycin in the treatment of CAP.

In summary, vancomycin remains a commonly prescribed antibiotic for the treatment of CAP, despite the rare occurrence of MRSA pneumonia. This study adds to a growing body of literature[3,4] that suggests empiric broad-spectrum antibiotic therapy for CAP is not only not beneficial to patients, but may be potentially harmful. Clinicians should think carefully before prescribing vancomycin for patients with CAP, and quickly deescalate antibiotics as clinical information develops.

References

1. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med.* 2019;200(7):e45-e67.
2. Jones BE, Ying J, Stevens V, et al. Empirical Anti-MRSA vs Standard Antibiotic Therapy and Risk of 30-Day Mortality in Patients Hospitalized for Pneumonia. *JAMA Intern Med.* 2020;180(4):552-560.
3. Webb BJ, Sorensen J, Jephson A, Mecham I, Dean NC. Broad-spectrum antibiotic use and poor outcomes in community-onset pneumonia: a cohort study. *Eur Respir J.* 2019;54(1).
4. Attridge RT, Frei CR, Restrepo MI, et al. Guideline-concordant therapy and outcomes in healthcare-associated pneumonia. *Eur Respir J.* 2011;38(4):878-887.