Ontario Antimicrobial Stewardship Project

Evidence-Based Summary for Short-Course Antimicrobial Therapy:

Ventilator-associated Pneumonia (VAP)

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1. *Treatment with a total of 8 days of adequate antimicrobial therapy for proven VAP is appropriate. Because of higher rates of relapse with infections due to P. aeruginosa or mdr- Acinetobacter spp. consider extending duration to 15 days.*

   A randomized controlled trial in 197 patients with VAP compared 8 days versus 15 days of antibiotic treatment. (2) Patients were included if they were intubated with mechanical ventilation for >48 hours, had positive cultures (distal pulmonary secretion samples, BAL or protected specimens), a diagnosis of VAP (new infiltrate on chest radiograph and either purulent tracheal secretions, a temperature of >38.3°C or a leukocyte count >10000/uL), and were started on appropriate empirical antibiotic therapy.(2) Exclusion criteria were pregnancy, a SAPS II score >65 points, neutropenia, AIDS, had received stage 3 immunosuppression or long term steroids, concomitant extra pulmonary infection, bacteremia or shock.(2) Empirical antibiotic selection was left to the discretion of the treating physician, but the preferred regimen was initially an aminoglycoside or fluoroquinolone plus a broad spectrum beta-lactam, then targeted therapy after 48-72 hours. Overall at day 28 of follow-up, 8 days of therapy was found to be non-inferior to 15 days of therapy for all cause mortality and microbiologically documented infection recurrence rate.(2) Secondary endpoints also demonstrated no significant differences in 60 day mortality, length of stay in the ICU or hospital, or number of days ventilated.(2) For primary infections caused by non fermenting gram-negative bacilli i.e. *Pseudomonas aeruginosa* or *Acinetobacter spp.*, a higher percentage of patients in the group treated with 8 days developed pulmonary infection recurrence. It would therefore be prudent to continue therapy for a total duration of 15 days in patients when these are isolated.

2. *Patients with suspected VAP should be reassessed at 96h and their antibiotics discontinued if CPIS score is <6. Other early discontinuation strategies for patients with suspected VAP may be effective.*

   Evidence-based clinical practice guidelines for ventilator-associated pneumonia(1), developed by the Canadian Critical Care Trials Group recommend the use of an antibiotic discontinuation strategy based on clinical criteria, concluding that this shortens the duration of antibiotic therapy with no adverse effects on clinical outcome.

   An antibiotic discontinuation strategy such as the clinical pulmonary infection score (CPIS) was demonstrated to shorten the duration of antibiotics.(3) The clinical CPIS includes criteria of temperature, blood leukocytes, tracheal secretions, oxygenation, pulmonary radiography, progression of pulmonary infiltrate, and culture of tracheal aspirate.(Appendix) A randomized controlled trial allocated 81 patients to either an intervention group who received IV ciprofloxacin and evaluation at 3 days with the CPIS score, where if the CPIS score was ≤6 the antibiotic was stopped, or a control group who received therapy with physician-directed antibiotics.(3) There was no significant difference between the groups with respect to mortality.(3) Patients in the intervention group did have statistically fewer days on antibiotics, shorter ICU stays, and lower incidence of antimicrobial resistance or super infections.(3)

3. *Appropriate single agent therapy is recommended for each potential pathogen as empiric therapy for VAP, when appropriate for local resistance patterns.*

   The guidelines developed by the Critical Care Trials Group (1) also recommend appropriate single agent therapy for each potential pathogen as empiric therapy for VAP. Based on 5 trials, they were able to conclude that empiric broad-spectrum combination therapy had no advantage over monotherapy with respect to differences in mortality or clinical response rates (1). This use of monotherapy as recommended is another strategy for efficient use of antimicrobial therapy.

References

1. Muscedere J, Dodek P, Keenan S, Fowler R, et al. Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: Diagnosis and Treatment. Journal of Critical Care. 2008;23:138-47.
2. Chastre J, Wolff M, Fagon JY et al. Comparison of 8 vs. 15 Days of Antibiotic Therapy for Ventilator-Associated Pneumonia in Adults: A Randomized Trial.
3. Singh N, Rogers P, Atwood C, et al. Short-course Empiric Antibiotic Therapy for Patients with Pulmonary Infiltrates in the Intensive Care Unit. Am J Respir Crit Care Med. 2000;162:505-511.

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Appendix

Clinical Pulmonary Infection Score Calculation (3)

Temperature (ºC)
- ≥ 36.5 and ≤ 38.4 = 0 points
- ≥ 38.5 and ≤ 38.9 = 1 points
- ≥ 39 and ≤ 36 = 2 points

Blood leukocytes,mm^3
- ≥4000 and ≤ 11000 = 0 points
- <4000 and > 11000 = 1 point + band forms ≥50% = add 1 point

Tracheal secretions
- Absence of tracheal secretions = 0 points
- Presence of nonpurulent tracheal secretions = 1 point
- Presence of purulent tracheal secretions = 2 points

Oxygenation: $Pa0_2/Fi0_2$ mmHg
- >240 or ARDS (ARDS defined as $Pa0_2/Fi0_2$ >200, pulmonary arterial wedge pressure ≤ 18mmHg and acute bilateral infiltrates) = 0 point
- ≤ 240 and no ARDS = 2 points

Pulmonary radiography
- No infiltrate = 0 point
- Diffuse (or patchy) infiltrate = 1 point
- Localized infiltrate = 2 points

Progression of pulmonary infiltrate
- No radiographic progression = 0 points
- Radiographic progression (after CHF and ARDS excluded) = 2 points

Culture of tracheal aspirate
- Pathogenic bacteria* cultured in rare or light quantity or no growth = 0 point
- Pathogenic bacteria cultured in moderate or heavy quantity = 1 point
- Same pathogenic bacteria seen on Gram stain, add 1 point

Definition of abbreviations: ARDS = acute respiratory distress syndrome; CHF = congestive heart failure; $Pa0_2/Fi0_2$ = ratio of arterial oxygen pressure to fraction of inspired oxygen.
*Predominant organism in the culture