Dilemmas in Ventilator- and Hospital-Acquired Pneumonia

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No conflicts to disclose

Topics

• Prevention, diagnosis, and treatment of ventilator-associated pneumonia (VAP)
• What to do with ventilator-associated tracheobronchitis?
• Hospital-acquired pneumonia (HAP) in the non-ventilated patient
• How long do you treat VAP/HAP?
Case vignette #1

• You are a hospitalist at a small community hospital, recently appointed to be the medical director of a mixed medical-surgical ICU. Upon reviewing the past year’s case records, you realize that your ICU has an unacceptably high prevalence of ventilator associated-pneumonia (VAP).

As the ICU director, you should prioritize all except:
1. Ventilator “bundles” designed to prevent VAPs
2. Protocols to decrease length of mechanical ventilation
3. Oropharyngeal care with chlorhexidine
4. Protocolized decontamination of gastrointestinal flora

VAP vs. HAP vs. HCAP

• Ventilator associated pneumonia:
  – Pneumonia occurring > 48 hours after intubation
• Hospital acquired pneumonia:
  – Defined as a non-ventilator-associated pneumonia occurring > 48 hours after admission
• Health care-acquired infection (HCAP):
  – No longer recognized in 2016 IDSA/ATS criteria (Kalil AC et al. Clin Infect Dis 2016)
  • Evidence does not support that health care exposure imparts risk for multidrug infection

Burden of VAPs

• Lambert et al. Lancet Infect Dis 2011
  – 120,000 patients admitted to 537 ICUs in Europe
  • 7% rate of VAPs
  • VAP: 2.3 fold increased risk of mortality, increased LOS
  • Outcomes only modestly worsened by drug resistance
• Melson et al. Lancet Infect Dis 2013
  – VAP decreases daily chance of discharge by 26%
  – Attributable mortality varies!
  • All patients: 13% attributable mortality
  • Post-surgery patients: 69% attributable mortality
  • Medical ICU patients: 0% attributable mortality
Prevention of VAP?

1. Decreasing time on the ventilator
2. Minimizing aspiration of oral flora
3. Effectively implement changes (i.e. bundles)

Decreasing ventilator time

  - Minimize sedation
    - Bolus preferred to continuous (50% decrease in vent days) Brook et al. Crit Care Med 1999
    - Daily sedation cessation with superimposed spontaneous breathing trials (3 fewer vent days) Girard et al. Lancet 2008
  - Respiratory therapist-run weaning protocols
    - 1.5 fewer vent days (NEJM 2000); fewer trauma VAPs Marelich Chest 2000
  - Early tracheostomy?
    - Decreases vent time; no change in VAP rates Terragni et al. JAMA 2010

Minimizing aspiration of oral flora

- VAPs arise from aspiration of oral contents
  - Oral decontamination
    - 2% chlorhexidine favored in metaanalysis Labbeau et al. Lancet Infect Dis 2011
    - Providone-iodine may be harmful Seguin P Crit Care Med 2014
    - No benefit from whole-body chlorhexidine bathing Noto MJ JAMA 2015
  - Head-of-bed elevation Drakulovic Lancet 1999
  - Antibiotic decontamination of digestive tract?
    - Controversial; drug resistance? Maselli Ther Adv Respir Dis 2011
Implementing change in the ICU

ICU Bundles—“A group of evidence-based interventions that, when implemented together, result in better outcomes than when implemented individually” (Chittick Crit Care Med 2010)

• Ventilator bundles
  – Hand hygiene, gowns
  – Head of bed elevation > 30-45°
  – ETT cuff pressure > 20 cm H₂O
  – Chlorhexidine oral care
  – Avoiding nonessential vent tubing changes

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Case vignette #2

It is Monday morning after a hectic weekend in the ICU. You and your respiratory therapist are discussing Mr. M, a 60 year old male on ventilator day 5 for COPD exacerbation. You are debating whether Mr. M developed a ventilator-associated pneumonia over the weekend.

According to the CDC’s new “ventilator-associated event surveillance system”, what is needed to diagnose a probable VAP?

- (A) A change in quality and quantity of sputum production
- (B) Mandatory sampling of respiratory secretions with bronchoalveolar lavage
- (C) Chest imaging (2-view or CT) showing new parenchymal infiltrates
- (D) Antibiotic use for infection-related ventilator-associated complications
Ventilator associated pneumonia

- Pneumonia occurring > 48 hours after intubation
  - Accounts for most hospital-acquired pneumonias
    - Major outcome targeted by ICU quality improvement initiatives
- Classically defined by triad of new CXR infiltrate, worsening oxygenation, change in sputum

Challenges in diagnosing/tracking VAP

- Criteria are nonspecific/qualitative
  - What constitutes an infiltrate on CXR?
  - What constitutes a change in sputum consistency?
  - What constitutes worsened oxygenation?
- Ample motive for bias in VAP reporting
  - Financial penalties for having VAPs
  - 50% of non-teaching ICUs in US report VAP incidence of 0% (Dudzik et al. Am J Infect Control 2011)
    - Despite a 15% prevalence of antibiotics given for nosocomial pneumonia (Klompas NEJM 2013)
  - Europe (fewer financial disincentives): 7% rate of VAPs (Lambert et al. Lancet Infect Dis 2011)

New criteria for diagnosing ventilator “events”

<table>
<thead>
<tr>
<th>Concept</th>
<th>Name</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>New</td>
<td>ventilator-associated</td>
<td>Change in respiratory status</td>
</tr>
<tr>
<td>abnormal</td>
<td>condition (VAC)</td>
<td>New respiratory deterioration with evidence of infection (CDC)</td>
</tr>
<tr>
<td>abnormal</td>
<td>condition</td>
<td>Increasing evidence of pulmonary infection on sputum sampling (Klompas)</td>
</tr>
<tr>
<td>abnormal</td>
<td>condition</td>
<td>Antibiotic initiation (Klompas)</td>
</tr>
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<td>condition</td>
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</tr>
</tbody>
</table>
Implications at the bedside?

- CDC: Diagnosis largely hinges on retrospective decision to treat infection (Klompas NEJM 2013)
  - Avoids radiographic, subjective (sputum quality) tests susceptible to biased reinterpretation (“Monday morning quarterbacking”)
  - Doesn’t really help you prospectively at the bedside
    - Circuitous logic:
      - A diagnosed pneumonia should be treated with antibiotics
      - Antibiotic treatment is needed to diagnose the pneumonia
    - Surveillance criteria, not diagnostic criteria

Implications at the bedside?

- Still left with old VAP criteria to determine if to treat
  - Change in infiltrate
  - Worsening respiratory status
  - Sputum evidence of infection
    - IDSA/ATS 2016: Tracheal aspirate (with semiquantitative cultures) preferred over bronchoalveolar lavage quantitative cultures
      - Sample technique does not influence clinical outcomes (Berton DC Cochrane Database Syst Rev 2014)

What antibiotics are used for VAP?

Step One: Determine risk for MDR infection
- IV antibiotics in last 90 days
- Septic shock or ARDS at time of VAP onset
- Hospitalized > 5 days prior to VAP onset
- On hemodialysis at time of VAP onset

Step Two: Tailor antibiotic regimen
- Default regimen should cover MSSA, Pseudomonas, other gram (-)'s, shaped to local “antibiogram”
- If MDR risk high, or if ICU MRSA rate > 20%, cover MRSA
- If MDR risk high, or if ICU gram (-) resistance rates > 10%, 2x cover Pseudomonas

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Case vignette #3
Mrs. W has been intubated for 10 days for respiratory failure due to Guillain Barré syndrome. She develops a new fever, purulent sputum (gram positive cocci on gram stain), yet has no radiographic infiltrate. Otherwise remains clinically stable.

How would you proceed with Mrs. W?
1. Treat for VAP with empiric antibiotic coverage dictated by MDR risk (MRSA, pseudomonas)
2. Treat for ventilator-associated tracheobronchitis, guided by sputum culture
3. Don’t treat

Ventilator-associated tracheobronchitis
- Ventilated patient with fever (without other cause), change in sputum, positive sputum culture, but no change in oxygenation or chest radiograph
  - Typically polymicrobial; 61% MDR (Kalil AC et al. Clin Infect Dis 2016)
  - Most common organisms:
    - P. aeruginosa (34%)
    - MRSA (32%)
    - Acinetobacter (27%)
    - Klebsiella (5%)
Ventilator-associated tracheobronchitis

- Nseir S et al. *Crit Care* 2008
  - 58 pts randomized to IV abx (8 days) vs. no abx
    - Abx improved rate of VAP development; decreased ICU mortality (18% vs. 47%)!
      - Study stopped early at interim analysis
- Four observational studies? (Kalil AC et al. *Clin Infect Dis* 2016)
  - IV abx decreased time on ventilator (3.5 fewer days); no effect on other outcomes
- IDSA/ATS recommendations: Do not treat VAT

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Hmm......

- IDSA/ATS 2016: “In patients with VAT, we suggest not providing antibiotic therapy (*weak recommendation, low-quality evidence*)”
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**Case vignette #4**

J.G. was admitted for 7 days to your general medical ward for the management of alcoholic hepatitis and spontaneous bacterial peritonitis. On the day of planned discharge, he develops cough, fever, and hypoxia. A CXR reveals a new right lower lobe infiltrate.

Which of the following are true about J.G.:

1. His hospital acquired pneumonia could have been prevented using VAP-mitigating techniques
2. He should be double-covered for resistant gram negative infection
3. He can be treated with quinolone monotherapy
4. Post-pyloric feeding would have decreased his HAP risk

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**HAP in non-intubated patients**

Pneumonia within 48 h of hospitalization

- 50% complication risk (sepsis, empyema, etc)
- 13.9% attributable mortality (Sopena et al. Chest 2005)

Causative flora?

- S. pneumoniae, Legionella major causes in non-ICU patients (Sopena et al. Chest 2005)
- ICU patients unknown

Antibiotic treatment should be tailored to hospital's flora
Treatment for HAP: 2016 IDSA guidelines

Treatment options depend upon:

1. Risk of mortality
   - High risk: respiratory failure, septic shock, etc.

2. Risk of MRSA
   - High risk: local flora with > 20% MRSA prevalence, or unknown prevalence

3. Receipt of IV antibiotics in previous 90 days

4. Presence of structural lung disease (bronchiectasis)

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Can HAP be prevented?

VAP preventative techniques?

• Head of bed elevation
  – No studies in non-intubated patients

• Chlorhexidine oral care
  – No clear benefit in non-intubated patients (Panchabhai et al. Chest 2009)
Can HAP be prevented?

- Stress ulcer prophylaxis (Marik et al. Crit Care Med 2010)

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Case vignette, continued (#5)

- You begin J.G. on broad-spectrum antibiotics and treat him for sepsis. Sputum gram stain reveals gram positive cocci; cultures are pending.

How long should you continue antibiotic therapy?
1. 3 days of therapy
2. 7 days of therapy
3. 14 days of therapy
4. Stop at day 1 if procalcitonin < 0.5 ng/ml

Rapidity of antibiotic effect

- Clinical benefits of treatment are typically achieved within 6 days of therapy (Luna et al. Crit Care Med 2003)
- 8 days of VAP treatment equivalent to 15 days of treatment (Chastre et al. JAMA 2003)
  - 15 days preferred for Pseudomonas, Acinetobacter due to decreased recurrence
- Duration > 14 days increases colonization risk (ATS/IDSA 2005)
- No data for non-ventilator HAP

Meta-analyses

- Pugh R et al. Cochrane Database Syst Rev 2015
  - 7-8 days of antibiotics (as opposed to 10-15 days) associated with reduced antibiotic usage, fewer multidrug resistant VAPs, no differences in other outcomes
    - Increased risk of recurrent infection, unclear significance
- Dimopoulos G et al. Chest 2013
  - Fewer antibiotic days with short-term treatment; no other differences (good or bad)
  - Fewer antibiotic days, no differences in recurrent infection

All analyses heavily biased towards VAP (few patients with HAP included)
Can we stop antibiotics even earlier?

- **Procalcitonin**
  - Protein typically only produced in thyroid
    - During infection, expressed/released by all tissues
  - Procalcitonin thresholds for VAP antibiotic cessation
    - Stoltz *et al.* *ERJ* 2009: 72 h procalcitonin < 0.5 ng/ml (or decrease of 80% from baseline) indicated ability to safely stop antibiotics. Decreased abx days by 3.
    - Bouadma *et al.* *Lancet* 2010: Similar findings with all ICU infections (including VAP), could stop abx at day 3

Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial *Lancet Infect Dis* 2016

- 1575 ICU patients with any infection (25% HAP/VAP) randomized to procalcitonin-guided antibiotic de-escalation (80% drop or < 0.5 ng/ml at day 3) vs. standard care (test performed, provider not informed)
  - Providers were reticent about stopping antibiotics (took 1-2 days after criteria met)
  - Procalcitonin group had fewer antibiotic days, decreased 28-day (19.6% vs. 25%) and 1-year (34.8% vs. 40.9%) mortality

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