American College of Surgeons Critical Care Review Course 2012

Syllabus: Ventilator-Associated Pneumonia

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I. Definition

A. General definition: Bacterial infection of the lung involving inflammation and consolidation of lung tissue, and associated with being on a mechanical ventilator

B. CDC definition: pneumonia arising during or within 48 hours of endotracheal intubation

C. Definition vs. diagnosis

1. Definition is clear, diagnosis is often empirical

2. General diagnosis: growth of bacteria from a culture of lower respiratory tract secretions in the setting of clinical signs and symptoms of infection

3. lack of universally applicable, sensitive, specific, and validated diagnostic criteria

II. Pathogenesis

A. aspiration and migration of oropharyngeal secretions into the airways

1. leakage around endotracheal tube cuff

2. direct aspiration into the airways

3. colonization of the biofilm on the endotracheal tube

4. secondary infection from the bloodstream (uncommon)

B. Causative organisms

1. early time period and new hospital admission

a. Staph, Strep, Hemophilus predominate

2. after 4 days in ICU/intubated or with recent healthcare facility admission

a. Gram negatives more frequent, Pseudomonas, E. coli

b. MRSA

c. more multi-drug resistant organisms (MDRO)

3. Staph aureus most common pathogen overall (MSSA > MRSA)

a. local hospital and ICU bacteriology varies

4. Pseudomonas most common Gram negative pathogen

III. Epidemiology

A. Incidence of VAP

1. variable depending on patient population, hospital, ICU

2. 10 - 20% based on most studies in the last 20 years

B. VAP rates

1. National Healthcare Safety Network (NHSN) of the CDC does VAP surveillance at hospitals across the country and reports VAP rates as “rate per 1000 ventilator days”

2. NHSN rates vary according to type of ICU (2006 – 2008 data)

a. Medical 2.2/1000 ventilator days

b. Surgical 4.9/1000 ventilator days

c. Trauma 8.1/1000 ventilator days

3. The relative rates reported for different patient populations has consistently shown the sequence from lowest to highest as Medical < Surgical < Trauma

4. NHSN rates are surveillance rates (i.e. captures patients who meet one set of criteria) and are not equivalent to the actual rates of VAP as diagnosed by clinicians

IV. Diagnostic methods

A. Clinical strategy

1. New or progressing pulmonary infiltrate on radiologic study, plus $\geq$ 2 of the following: fever/hypothermia, leukocytosis/leucopenia, purulent sputum, decline in oxygenation

2. These criteria are not defined further (nonspecific); e.g. what is “purulent”?

3. Sensitivity decreases and specificity increases as more of the 5 criteria are included in diagnosis

4. Tends to be oversensitive, leading to more antibiotic therapy

5. Diagnosis supported, but not confirmed, by bacterial growth on semi-quantitative culture

a. semi-quantitative: reports light, moderate, or heavy growth

b. after 4 days of intubation, upper airways become colonized with bacteria; growth from endotracheal sputum aspirate does not necessarily reflect presence of alveolar or lung parenchymal infection

6. Diagnosis excluded with high negative predictive value by a negative culture (i.e. no growth) in patients not already on antibiotics (within 72 hours) and not septic

7. Clinical strategy confounded by noninfectious processes that may mimic pneumonia

a. pulmonary, contusion, edema, or embolism; aspiration pneumonitis; ARDS; atelectasis, drug reaction

B. Bacteriologic strategy

1. Uses quantitative cultures of the lower respiratory tract and growth at a certain threshold

a. quantitiative: reported as number of colony-forming units/mL (e.g. 10^3, 10^4, or 10^5)

2. Often employs invasive culture techniques:

a. bronchoalveolar lavage (BAL), by bronchoscopy or non-bronchoscopic blind catheter

b. protected specimen brush (PSB)

3. Advantages of bacteriologic strategy

a. less overall antibiotic use

b. induces a change in antibiotic choice more frequently than the clinical strategy (more targeted to causative organisms)

c. culture obtained from specific lung segments (location of infiltrate)

d. allows therapeutic suctioning when bronchoscopy used

4. Conflicting evidence of whether an outcome benefit (reduced mortality) is seen with bacteriologic strategy

V. Controversies of diagnosis

A. Clinical vs. pathologic

1. diagnosis of VAP based on clinical criteria is subjective, and often inaccurate when compared to a tissue biopsy diagnosis

2. one third of patients who die with a clinical diagnosis of VAP have no evidence of pneumonia on autopsy

3. one fourth of mechanically ventilated patients who die without a diagnosis of VAP do have evidence of pneumonia on autopsy

4. one autopsy study showed that a clinical diagnosis had a 69% sensitivity and 75% specificity when compared to postmortem histology

B. Clinical vs. bacteriologic

1. in trauma patients, one study showed that only 39% of patients who met clinical criteria for VAP had VAP based on BAL with quantitative cultures

C. Quantitative threshold

1. The optimum threshold has not been defined

2. $>10^4$ CFU/mL usually used in medical and nontrauma surgical patients; $>10^5$ CFU/mL often used in trauma patients

a. 10^4 threshold may result in treating patients that do not really have VAP

b. 10^5 threshold results in a false negative rate of 10 – 15%, i.e. patients with growth between 10,000 and 100,000 CFU who have VAP but are not treated

i. use of the 10^5 threshold in trauma patients has not been associated with excess mortality or recurrence

c. the CDC uses 10^4 as the diagnostic threshold regardless of the method used (bronchoalveolar lavage, protected specimen brush, or non-bronchoscopically obtained deep specimens)

d. sensitivity of culture is decreased if cultures taken while patients are already on antibiotics

i. convention is to drop the threshold by a factor of 10, i.e. if 10^5 is the chosen threshold, use 10^4 if culture taken concurrently with antibiotic use

VI. VAP Prevention and Risk factors

A. Few interventions or processes directly reduce VAP rates

1. prevention best accomplished by application of the few directly proven techniques (see VI.C.1.a.), adoption of other related best practices that indirectly influence risk of VAP, and avoidance of risk factors

B. Risk factors for VAP may be broadly classified as modifiable or non-modifiable

1. modifiable: factors that are subject to changes in practice based on current evidence that can impact the degree of risk for VAP

2. non-modifiable: factors which persist despite implementation of the best current evidence, or which cannot be modified except at the expense of other practices which provide greater benefit

C. Modifiable risk factors

1. Ventilator-related processes that may reduce VAP rates

a. directly decrease VAP risk by decreasing aspiration

i. semirecumbent positioning (head of bed >30 degrees)

ii. keep endotracheal cuff pressures >20 cm H2O

iii. continuous subglottic aspiration for intubated patients

b. decrease VAP risk indirectly by decreasing time on ventilator

i. avoid endotracheal intubation in the first place

ii. earlier extubation

iii. daily assessment for extubation with spontaneous breathing trials

iv. daily sedation interruption protocol

v. use of a ventilator weaning protocol

vi. preventing unplanned extubation (e.g. self-extubation)

vii. decreasing reintubation rates

2. General processes that may reduce VAP rates

a. appropriate blood transfusion practices

i. each unit of PRBC and FFP increases VAP risk

b. appropriate use of stress ulcer prophylaxis

c. oral chlorhexidine rinses

d. early mobilization out of bed

e. avoiding inappropriate or unnecessary antibiotics

f. glucose control

g. hand hygiene

h. ICU staff education about VAP reduction

i. appropriate ICU staffing ratios

j. early tracheostomy in trauma patients (possibly)

D. Non-modifiable risk factors

1. aspiration in the prehospital setting
2. blood transfusion for hemorrhage resuscitation
3. coma and severe traumatic brain injury
4. emergent intubation in prehospital setting or upon initial presentation
5. contraindication/inability to raise head of bed
    i. unstable spinal injury
    ii. open abdomen with loss of domain
6. age >60
7. ARDS

E. Other

1. Selective gut decontamination
    a. reduces VAP rates, but not recommended for routine use
    b. benefit mostly seen where MDRO rates were very low
    c. may increase infections with MDRO
2. Antibiotic cycling
    a. may have benefit in preventing MDRO
    b. VAP reduction not proven

VII. Treatment

A. Antibiotic therapy

1. early empiric antibiotics (abx)
    a. Mortality is significantly increased when
        i. abx initiation is delayed (hours matter)

ii. initial abx are inadequate (do not cover the causative pathogen)

iii. when initial abx inadequate, changing to adequate coverage after cultures return results in same excess mortality

b. abx are initiated upon suspicion of VAP

i. before cultures are resulted and preferably before cultures are taken

ii. cultures done while on abx are less sensitive for infection

c. empiric abx choice

i. ideally based on local ICU-specific antibiogram

ii. MRSA coverage (vancomycin or linezolid)

iii. other Gram positive and Gram negative coverage, including Pseudomonas and local MDROs

iv. must be dosed properly; empiric dose for VAP may be higher than "normal" treatment dose

2. de-escalation

a. de-escalation = narrowing abx treatment to one drug with narrowest spectrum of activity that adequately treats the causative pathogen

b. select abx with low MIC (minimum inhibitory concentration values)

c. no benefit of double-coverage of Pseudomonas

d. no benefit of combination therapy if one drug covers causative pathogen

e. continued broad abx use may lead to selection of MDROs

3. Length of treatment

a. 3 randomized studies on duration of abx for VAP

i. 7 or 8 days is as effective as longer courses

1. reduces abx days

2. reduces recurrent infection with MDRO

3. no difference in recurrence, except with non-fermenting Gram negative bacilli

ii. if VAP from non-fermenting Gram negative bacilli (Pseudomonas, Acinetobacter, Stenotrophomonas) VAP recurrence rate higher; otherwise, comparable outcomes

b. use of a clinical resolution treatment end point

i. stopping abx when fever, leukocytosis, hypoxemia, purulent sputum, and infiltrate resolve

ii. decreased abx days; no adverse outcomes

c. discontinuation of treatment based on procalcitonin level

i. procalcitonin: prohormone, specifically increases in response to bacterial infection, decreases with infection resolution

ii. studies suggest reduce abx exposure with no adverse outcomes