

# Antibiotic therapy for VAP

## Three points will be discussed:

1. The initial antimicrobial treatment
2. The therapeutic strategies when the clinical situation is evaluated and bacteriological data are available
3. The duration of treatment

# Adequate antibiotic therapy

- defined as the administration of at least one antibiotic at an appropriate dose to which the isolated organisms are sensitive

# The initial antimicrobial treatment

- Prompt initiation of antibiotic therapy is a cornerstone of treatment of VAP

# The initial antimicrobial treatment

- Changing antimicrobial therapy once culture results are available does not appreciably reduce the excess mortality associated with inadequate initial therapy

*Luna CM et al. Impact of BAL data on the therapy and outcome of VAP. Chest 1997; 111:676-685*

*Alvarez-Lerma F. Modification of empiric antibiotic treatment in patients with pneumonia acquired in ICU. Intensive Care Med 1996;22:387-394*

*Kollef MH et al. The influence of mini-BAL cultures on patient outcomes . Chest 1998;113:412-420*

*Rello J et al. The value of routine microbial investigation in VAP. Am J Respir Crit Care Med 1997;156:196-200*

# Clinical importance of delays in the initiation of appropriate antibiotic treatment for VAP

*Iregui M et al. Chest 2002; 122:262-268*

- Of the 107 patients treated for VAP, 33 patients received delayed but adequate treatment while 74 patients received adequate treatment in a timely manner
- Delay was associated with a sig. increase in hospital mortality (69.7% vs 28.4% with  $p < 0.01$ )

# Clinical importance of delays in the initiation of appropriate antibiotic treatment for VAP

*Iregui M et al. Chest 2002; 122:262-268*

- The delayed group received antibiotics approximately 16 h later than the group not delayed ( $28.6 \pm 5.8\text{h}$  vs  $12.5 \pm 4.2\text{h}$ )
- The narrow time frame may explain the finding that changing antibiotics once culture results are available does not reduce the excess mortality associated with inadequate initial therapy

# Choice of initial antibiotic/s

- Ideally wide enough to cover all the potential causative pathogens yet not too wide to limit the emergence of resistance
- Based on the risk factors for multi-drug-resistant pathogens and the local hospital antibiogram

# Risk factors for MDR pathogens

- Antibiotics in the preceding 90 d
- Hospitalization in preceding 90 d
- Current hospitalization  $\geq 5$  d
- Duration of MV  $\geq 7$  d
- History of regular visits to an infusion or dialysis center
- Residence in a nursing home or extended-care facility
- Immunosuppressive disease or therapy
- High frequency of antibiotic resistance in the community or ICU

From American Thoracic Society and Trouillet et al

# Risk factors for MDR pathogens

- Duration of MV  $\geq 7$  days  
+ Prior antibiotic use  
( $<30$  days / VAP onset)  
especially important

*Trouillet JL et al. VAP caused by potentially drug-resistant bacteria. AM J Respir Crit Care Med 1998;157:531-539*

# Early onset VAP and no risk factor for multidrug-resistant causative pathogen

- Ceftriaxone or
- Ciprofloxacin or
- Ampicillin / sulbactam or
- Ertapenem

*American Society Society Documents. Guidelines for the management of adults with hospital-acquired, ventilator-associated and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005; 171:388-416*

## Late onset VAP or risk factor(s) for multidrug-resistant causative pathogen

- Antipseudomonal cephalosporin (cefepime, ceftazidime) or
- Antipseudomonal carbapenem (imipenem, meropenem) or
- B-lactam / B-lactamase inhibitor (pip-tazo)  
plus
- Antipseudomonal fluoroquinolone (ciprofloxacin) or
- Aminoglycoside (amikacin, gentamycin)  
plus
- Linezolid or vancomycin ( if risk factors for MRSA are present or if locally incidence of MRSA is high)

# Points to note in antibiotic therapy

- The antibiotics must be given in adequate amounts and at appropriate intervals
- In patients with impaired renal or hepatic function, the dose may have to be adjusted daily
- The dose may have to be redosed after procedures e.g. dialysis

# Evaluation after antibiotic initiation

- Clinical improvement usually takes 48-72h
- Antibiotics should not be modified during this time unless dictated by the results of microbiologic sensitivity data

# 4 different scenarios

- Clinical situation improves and cultures are positive
- Clinical situation improves and cultures are negative
- Clinical situation does not improve and cultures are positive
- Clinical situation does not improve and cultures are negative

# Clinical situation improves and cultures are positive

- Think of de-escalating strategy
- Adjust antibiotics according to sensitivity results

# Clinical situation improves and cultures are negative

- Consider stopping antibiotics

# Clinical situation does not improve and cultures are positive

- Adjust treatment if a pathogen resistant to the empiric antibiotic regimen is identified
- If all isolated pathogens are sensitive, search for other pathogens, complications, other diagnoses or other extrapulmonary sites of infection

# Clinical situation does not improve and cultures are negative

- Search for other pathogens, complications, other diagnoses or other extrapulmonary sites of infection
- Note that in the absence of antibiotics or of a change in antibiotic treatment in the previous 72 hours, a negative tracheal aspirate culture has a strong negative predictive value, ruling out the diagnosis of VAP

# Duration of therapy

- This paper threw some light to the duration of therapy

# Comparison of 8 vs 15 days of antibiotic therapy for VAP in adults: a randomised trial

Chastre J et al. JAMA 2003; 290:2588-2598

- An 8 day duration of treatment was associated with a similar outcome in terms of mortality, ventilator free days and LOS in ICU to a 15 day treatment

# Comparison of 8 vs 15 days of antibiotic therapy for VAP in adults: a randomised trial

Chastre J et al. JAMA 2003; 290:2588-2598

- Patients in whom VAP was due to *P aeruginosa* or *Acinetobacter* species had a greater risk of recurrence following discontinuation of antibiotics when treated for 8 days

# Duration of therapy

- In patients in whom there is a clinical suspicion of VAP but whose PSB or BAL culture results are negative at 3 days and who are clinically improving can safely have their antibiotics stopped

*Singh et al. Short course empiric antibiotic therapy for patients with pulmonary infiltrates in the ICU. Am J Respir Crit Care Med 2000; 162:505-511*

*Kollef MH et al. Antibiotic utilization and outcomes for patients with clinically suspected VAP and negative quantitative BAL cultures results. Chest 2005; 128:2706-2713*

*Fagon JY et al. Invasive and noninvasive strategies for management for suspected VAP: a randomised trial. Ann Intern Med 2000;132:621-630*

# Summary

- Start antibiotic(s) early once VAP is suspected
- Choose antibiotic(s) according to guidelines adapted at local level and updated as often as possible
- Re-evaluate at 48-72h with regard to de-escalation or withdrawal of treatment
- Finally when treatment is maintained, its duration should not exceed 8 days unless the causative pathogen is *Pseudomonas* or *Acinetobacter*