DOES AVAILABILITY OF HIGHER ANTIBIOTICS WILL HELP IN REDUCING MORTALITY IN VAP?

Dr. L. H. Ghotekar,

M.D; MNAMS;FICAM;FIMSA

Professor of Medicine

Lady Harding medical college

New Delhi, INDIA

L. H. Ghotekar*, Sumedh Dhuldhule**.

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VENTILLATOR ASSOCIATED PNEUMONIA (VAP)



Dr L H Ghotekar,

M.D; MNAMS;FICAM;FIMSA

Professor of Medicine

Lady Hardinge Medical College

New Delhi, INDIA

DEFINITIONS

- VAP- pneumonia that occurs 48–72 hours or thereafter following an endo-tracheal intubation.
- Early onset VAP: VAP that occurs within 4 days of intubation. Usually caused by antibiotic sensitive organisms.
- Late Onset VAP: Occurs after 4 days of intubation. Caused by MDR pathogens

American Thoracic Society, Infectious Diseases Society of America. *Am J Respir Crit Care Med 2005, 171:388–416.*

VENTILATOR ASSOCIATED PNEUMONIA (VAP) - KEY POINTS -

- VAP is the 2nd most common nosocomial infection = 15% of all hospital acquired infections
- Incidence = 9% to 70% of patients on ventilators
- Increased ICU stay by several days
- Increased avg. hospital stay 1 to 3 weeks
- Mortality = 13% to 55%
- Added costs of $40,000 - $50,000 per stay

Centers for Disease Control and Prevention, 2003.

Rumbak, M. J. (2000). *Strategies for prevention and treatment.* Journal of Respiratory Disease, 21 (5), p. 321.

RISK FACTORS

Host related:

1. Underlying medical conditions
2. Immune suppression, Malnutrition
3. Advanced age
4. Level of consciousness
5. Number of intubations
6. Medications

American Thoracic Society, Infectious Diseases Society of America. *Am J Respir Crit Care Med 2005, 171:388–416.*

RISK FACTORS CONTD..

- **Device related:**

1. Prolonged mechanical ventillation
2. Reintubations
3. Use of humidifiers
4. Nasogastric/ orogastric tubes

- **Personnel related:**

1. Improper hand washing
2. Failure to change gloves

MICROBIOLOGY

- The type of organism that causes VAP usually depends on the duration of mechanical ventilation.
- Early onset VAP is usually caused by antibiotic sensitive organisms and **late** onset VAP by **MDR pathogens.**
- Reports of early onset VAP caused by MDR pathogens are increasing.

ORGANISMS

Early Onset VAP:

1. Pneumococcus
2. H. influenzae
3. MSSA
4. Enterobacter species
5. Proteus species
6. Klebsiella
7. E.Coli
8. Serratia

Afshari et al. *Crit Care 2012, 16:242–247*

ORGANISMS CONTD

Late onset VAP:

1. Methicillin Resistant Staph Aureus (MRSA)
2. Pseudomonas aeruginosa
3. Acinetobacter species
4. ESBL producing organisms

Afshari et al.*Crit Care 2012, 16:242–247*

ORGANISMS FOUND IN OUR STUDY

- In our study conducted in a tertiary care centre Lady Hardinge Medical college & S.S.K. Hospital in a metropolitan city-Delhi the following organisms were isolated:

1. Acinetobacter Baumannii (33.33%)
2. Pseudomonas Aeruginosa (21.66%)
3. E.coli (18.33%),
4. Klebseilla (13.33%),
5. Staph.aureus (8.33%),
6. H.Influenzae (5%) .

DIAGNOSIS OF VAP



DIAGNOSIS

- No universally accepted criteria available at present.
- The available methods lack both sensitivity and specificity for diagnosis.
- Daily bedside evaluation in conjunction with chest radiography can only be suggestive of the presence or absence of VAP, but does not define it.
- The American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) guidelines recommend obtaining lower respiratory tract samples for culture and microbiology.

K Iompas M.*JAMA 2013, 297:1583–1593.*

CLINICAL PULMONARY INFECTION SCORE (CPIS)

- CPIS takes into account clinical, physiological, microbiological and radiographic evidence to allow a numerical value to predict the presence or absence of VAP.
- Has scores ranging between zero-twelve.
- A score of 6 or more has a good correlation with the diagnosis of VAP.
- But sensitivity and specificity are only 65% and 64% respectively.

K Iompas M. Clinician's Corner: Does this patient have ventilator-associated pneumonia? *JAMA 2013, 297:1583–1593.*

Shan J et al .*Respir Care 2011, 56:1087–1094.*

CDC SURVEILLANCE CRITERIA

- Defines two entities-Possible VAP and Probable VAP.
- A period of at least 2 days of stable or decreasing ventilator settings followed by consistently higher settings for at least 2 additional calendar days is required before a patient can be said to have a *ventilator-associated condition* (VAC).
- Most common causes of VAC are pneumonia, pulmonary edema, atelectasis, or ARDS.
- Signs of infection/infl ammation classify the patient as an "Infection-related ventilator-associated complication," or IVAC.

N ational Healthcare Safety Network (NHSN) July 2013 CDC/NHSN Protocol Clarifi cations 2013, Available at: http://www.cdc.gov/nhsn/PDFs/pscManual/10-VAE_FINAL.pdf

- Patients with an IVAC and purulent secretions alone or pathogenic cultures alone have “possible pneumonia”.
- Those with both purulent secretions and positive quantitative or semiquantitative cultures have “probable pneumonia”.
- Probable pneumonia is also defined by suggestive histopathological features, positive pleural-fluid cultures, or diagnostic tests for legionella and selected viruses.
- Chest radiograph findings have been excluded in the new criteria because of their subjectivity.

Kalanuria *et al. Critical Care 2014, 18:208.*

TREATMENT OF VAP



TREATMENT

- Selecting the appropriate antibiotic depends on the duration of mechanical ventilation.
- An updated local antibiogram for each hospital and each ICU based on local bacteriological patterns and susceptibilities is essential to guide optimally dosed initial empiric therapy.
- De-escalation is the key to reduce emergence of resistance.

Masterton RG: Antibiotic de-escalation. *Crit Care Clin 2011, 27:149–162.*

TREATMENT CONTD..

Early onset VAP:

Cephalosporins:

- Ceftriaxone: 2 g daily;
- cefuroxime: 1.5 g every 8 hours;
- cefotaxime: 2 g every 8 hours.

Fluroquinolones:

- Levofloxacin: 750 mg daily;
- Moxifl oxacin: 400 mg daily.

Beta lactams:

- Ampicillin + sulbactam: 3 g every 8 hours

Carbapenems:

- Ertapenem 1gm daily.

Torr es A et al. *Intensive Care Med 2009,* 35:9–29.

LATE ONSET VAP(MDR ASSOCIATED)

Beta lactam antibiotic (anti pseudomonal cephalosporin or carbapenems or anti pseudomonal penicillin)

PLUS

Coverage for gram negatives (Aminoglycoside or Anti pseudomonal fluroquinolone)

PLUS

Coverage for MRSA (Vancomycin or Linezolid).

Dimopoulos G et al. *Chest 2013; 144:1759–1767.*

Torr es A et al. *Intensive Care Med 2009;* 35:9–29.

DOSAGES FOR LATE ONSET VAP

- Cefepime: 1–2 g every 8 hours; ceftazidime 2 g every 8 hours.
- Carbepenems- Imipenem + Cilastin: 500 mg every 6 hours or 1 g every 8 hours; Meropenem: 1 g every 8 hours
- Beta-lactam/beta-lactamase inhibitor - Piperacillin + Tazobactam: 4.5 g every 6 hours.
- Aminoglycoside- Amikacin: 20 mg/kg/day; Gentamicin: 7 mg/kg/day; Tobramycin: 7 mg/kg/day.

TREATMENT CONTD..

- Ciprofloxacin 400 mg every 8 hours; levofloxacin 750 mg daily.
- Vancomycin: 15 mg/kg every 12 hours
- Linezolid: 600 mg every 12 hours.
- Acinetobacter species respond best to Carbapenems (also active against ESBL positive Enterobacteriaceae), colistin, polymyxin B and ampicillin/sulbactam.

TREATMENT CONTD..

- Duration of treatment for early onset VAP is 8 days and longer for MDR associated VAP.
- Reassess the patient every day and failure to improve in 48-72 hours should reconsideration of appropriate regimen.

OUR STUDY

- **Aims & Objective-**
- To identify the associated local microbial flora &
- To evaluate the factors for high mortality rate of inpatients with VAP.

OUR STUDY

- **Material & Methods-**
- Prospective study in 60 adult aged between 18 - 80 years admitted in medical I.C.U of Lady Hardinge Medical College and Hospital, New Delhi
- from November 2013 to April 2015.
- The study population consisted of patients expected to be mechanically ventilated for more than 48 hours.
- CDC definition of VAP was followed for the diagnosis.
- The study protocol was approved by ethical committee of the institution.
- Patients with ARDS and not fulfilling above mentioned inclusion criteria were excluded from study.

OUR STUDY

- **Data Collection**
- A detailed history-taking and a thorough clinical examination of all cases was done.
- Followed by relevant investigations required to make a diagnosis.
- certain baseline characteristics of all the participants were recorded on a predesigned proforma after obtaining an informed consent in written.
- Written consent was obtained from relatives of patients.
- Variables related to diagnosis of VAP and other important parameters noted in ICU set up like CBC, PaO_2/FiO_2 ratio, character of tracheal secretions (purulent or not), and quantity of tracheal aspirates etc were recorded daily.

OUR STUDY

- Chest radiographs were regularly done and were interpreted by two observers blinded to clinical results.
- A clinical diagnosis pneumonia was suspected when patient showed[8]a
  - new, progressive or persistent (>24h) infiltrate on chest radiograph + one of these criteria met-
    - Fever> 38^0C [100.4^0F] without other recognized cause or Leucocytosis (> 12000/mm^3) or leukopenia (<4000 /mm^3) or
    - Purulent tracheobronchial secretions. An endotracheal aspirate[9,10] was obtained immediately following clinical suspicion.
    - Identification of the organisms was done by various biochemical tests as per the Clinical Laboratory Standards Institute (CLSI) guidelines.[11]

OUR STUDY- STATISTICAL ANALYSIS-

- Data was compiled and analyzed using Microsoft Excel 2007 and SPSS version 20 software.
- Categorical variables are expressed as frequencies and percentages. Continuous variables are presented as mean ± standard deviation.
- Tests of significance were applied using following tests to assess if difference is real or by chance - Chi-square test (with Yate's correction wherever needed) and difference of proportion were applied for qualitative analysis.
- Mean and standard deviation between two groups were compared by independent t tests.
- Analysis of variance (Anova F Test) with post-hoc Tukey HSD (Tukey's honestly significant difference) was used to compare means between three or more groups.
- Association between two continuous variables was assessed by correlation analysis.
- Other relevant tests were applied, as needed in the study.

OUR STUDY- RESULTS

- Out of 60 cases 40, 20 were male and females respectively.
- The mean age for development of VAP was 49.30 ± 13.28 years and 42.1 ± 14.35 respectively with p value 0.0588.
- The mean BMI for patient was 20.88 ± 2.33 kg/m^2.
- Acinetobacter baumannii was found to be most predominant isolate (33.33%) followed by Pseudomonas aeruginosa (21.66%), E.coli (18.33%), Klebseilla (13.33%), Staph.aureus (8.33%), H.Influenzae (5%) .

OUR STUDY

- Pseudomonas aeruginosa showed highest sensitivity to Imipenem (86.62%), colistin (86.62%) followed by Meropenem (76.92%), Piperacillin-tazobactam (61.54%), vancomycin (61.54%), Gentamycin (53.54%) and Levofloxacin (53.54%).
- Acinetobacter *was* sensitive to antibiotics in the order Colistin, Imipenem, Meropenem, Linezolid, Amikacin, Vancomycin, Levofloxacin, Ceftriaxone (70%), Piperacillin-Tazobactam (60%) and, Gentamicin (60%).
- Klebsiella were most sensitive to Imipenem (75%), Meropenem (75%), Piperacillin–Tazobactam (75%) Amikacin (62.5%), Levofloxacin (62.5%). Lesser sensitivity was observed to Ceftriaxone (37.5%), Ciprofloxacin (37.5%), Gentamycin (25%) and Cefixime (25%).

OUR STUDY

- MRSA were 100% sensitive to Linezolid and showed good sensitivity for Vancomycin (80%), Imipenem (60%) and lesser sensitivity to Piperacillin-tazobactam (40%) and Ciprofloxacin(40%).
- The most effective antibiotics for E.coli were Imipenem (81.81%), Meropenem (72.72%), Levofloxacin (63.63%)
- The E.coli was moderately sensitive to Piperacilin-Tazobactam (54.54%), Amikacin (54.54%) and Ciprofloxacin (45.45%).

OUR STUDY-KEY POINTS

- Acinetobacter was most predominant isolate in our study isolated from tracheal aspirate cultures of patients accounting for 33% of the cases with widespread resistance to various antibiotics.

- The incidence of early onset VAP in this study was found to be 26.66% and of late onset VAP was 73.33% with mortality as high as 81.82% in late VAP.

OUR STUDY-KEY POINTS

	EARLY VAP		LATE VAP	
PRESENT STUDY	INCIDENCE	MORTALITY	INCIDENCE	MORTALITY
	26.66%	25%	73.33%	81.82%
Gadani H et al[17]	27.02%	20%	72.97%	66.66%
Goel et al[12]	39.62%	23.80%	60.38%	59.37%

OUR STUDY-TAKE HOME MESSAGE

- Acinetobacter baumannii is an important pathogen associated with early as well as late onset pneumonia
- They are resistant to most of the first line antibiotic used in hospital setting-to Ceftazidime, Gentamycin, Amikacin, Ciprofloxacin AND gradually developing resistance to carbepenems .

ANTIBIOTIC SENSITIVITY PATTERNS IN OUR STUDY

- *Acinetobacter* showed a sensitivity to antibiotics in the order colistin, Imipenem, Linezolid, Amikacin, vancomycin, levofloxacin, Ceftriaxone (70%), Meropenem (60%), Piperacillin-Tazobactam (60%) and, Gentamicin (60%).
- *Pseudomonas aeruginosa* showed highest sensitivity to Imipenem (86.62%), colistin (86.62%) followed by Meropenem (76.92%), Piperacillin-tazobactam (61.54%), vancomycin (61.54%), Gentamycin (53.54%) and Levofloxacin (53.54%).

ANTIBIOTIC SENSITIVITY PATTERNS IN OUR STUDY

- *Klebsiella* were most sensitive to Imipenem (75%), Meropenem (75%), Piperacillin–Tazobactam (75%) Amikacin (62.5%), Levofloxacin (62.5%). Lesser sensitivity was observed to Ceftriaxone (37.5%), Ciprofloxacin (37.5%), Gentamycin (25%) and Cefixime (25%).

- *MRSA* were 100% sensitive to Linezolid and showed good sensitivity for Vancomycin (80%), Imipenem (60%) and lesser sensitivity to Piperacillin-tazobactam (40%) and Ciprofloxacin(40%).

- The most effective antibiotics for *E.coli* were Imipenem (81.81%), Meropenem (72.72%), Levofloxacin (63.63%) and moderately sensitive to Piperacilin-Tazobactam (54.54%), Amikacin (54.54%) and Ciprofloxacin (45.45%).
- ***It means there is an emergence of Resistance to these antibiotics developing fast.***

TAKE HOME MESSAGE FROM OUR STUDY

- *There is an emergence of Resistance to these antibiotics developing fast.*
- There is a need of proper protocol and guidelines to be followed in hospital depending of occurrence of microorganism & sensitivity pattern.
- **New need for newer ANTIBIOTICS for ESBL producing organism and for organisms resistant to present antibiotics.**

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