Original Article

Clinical, Microbiological and Mortality Profile in Ventilator-associated Pneumonia in a Tertiary Care Hospital in Western India

Ghanshyam B. Borisagar, Amit R. Dedun and Rajesh N. Solanki

Department of Pulmonary Medicine, B.J. Medical College and Civil Hospital, Ahmedabad (Gujarat), India

Abstract

Background. Ventilator-associated pneumonia (VAP) is a major cause of morbidity and mortality in patients on mechanical ventilation (MV). There is paucity of data in our country regarding incidence, crude mortality rate, clinical profile, microbiological organism profile, mortality in early and late onset VAP and mortality as well as appropriate antibiotic therapy in these patients.

Methods. The study involved patients above 15 years of age with clinical suspicion of VAP, receiving MV for more than 48 hours in intensive care unit of our hospital. Patients were without evidence of pneumonia on admission. Study patients were followed until they were successfully treated and discharged from the hospital or death.

Results. Out of 50 patients, 31 (62%) patients were in 4th to 6th decades of life. Incidence of VAP was 21% and crude mortality rate was 42%. Due to neurological conditions, 22 (44%) patients required MV. VAP developed in 38 (76%) patients within 15 days of initiation of MV. Mortality in late onset VAP was found to be twice as compared to mortality in early onset VAP. Mortality in inappropriately treated patients was significantly higher than that of appropriately treated patients.

Conclusions. The incidence of VAP increases with increase in duration of hospital stay. There is significant morbidity and mortality in mechanically ventilated patients of VAP; if not treated appropriately early.

[Indian J Chest Dis Allied Sci 2018;60:135-139]

Key words: Ventilator-associated pneumonia, Mechanical ventilation, Intensive care unit, Fiberoptic bronchoscopy.

Introduction

Ventilator-associated pneumonia (VAP) is a major cause of significant morbidity and mortality in patients receiving mchanical ventilation (MV) and is one of the most common intensive care unit (ICU)-acquired infections in mechanically ventilated patients. VAP occurs in 8% to 28% of patients mechanically ventilated for longer than 48 hours.[1] Because of this large disease burden and the resultant attributable morbidity and mortality, there is great interest in accurately diagnosing, treating, and preventing this complication. It has been observed that more critically ill patients tend to develop VAP, and there are patient-related, infection control-related and intervention-related risk factors for VAP. Most episodes of VAP are postulated due to aspiration of oropharyngeal secretions containing potentially pathogenic organisms. Aspiration of gastric secretions may also contribute to a less extent.[2]

Ventilator-associated pneumonia is classified as early-onset VAP and late-onset VAP depending on the duration of MV at the time of onset of VAP and there is microbiological difference in the commonly isolated micro-organisms in these two groups. The isolation of the causative organisms is imperative for an appropriate therapy as there is strong evidence of the adverse effect of inadequate empirical treatment on outcome in patients of VAP.[3] The early and accurate diagnosis of VAP is a challenge and requires a rational and evidence-based medicine approach to institute rational and optimal management and antibiotic therapy.

The efficacy of diagnostic and preventive strategies is controversial. Diagnosis by invasive methods requires considerable commitment of resources; but can potentially reduce the cost of care in the long run; however, mortality benefit from this approach has not been demonstrated.[4] Prompt administration of appropriate antibiotics seems to be the only intervention that alter the outcome once the diagnosis is established.

Currently, there is no standard test for the diagnosis of VAP and no standardised methodology to exclude pulmonary infections in mechanically ventilated patients with fever and multi-organ dysfunction syndrome or multi-organ failure. Even

---

[Received: December 12, 2016; accepted after revision: December 6, 2017]

Correspondence and reprint requests: Dr Amit R. Dedun, Assistant Professor, Department of Pulmonary Medicine, B.J. Medical College and Civil Hospital, Ahmedabd-380 016 (Gujarat), India; E-mail: amitonly007@gmail.com

the post-mortem histological diagnosis of VAP is uncertain.[5] The bronchoscopic methods, *viz.* bronchoalveolar lavage (BAL) and protected specimen brush (PSB) are well established techniques and are increasingly being widely accepted invasive diagnostic techniques for identifying the aetiological pathogen of VAP. Previously, the impracticability of bronchoscopic methods in ICUs and also their cost had led to other strategies in clinical use, such as non-bronchoscopic techniques with catheters or mini-lavage.

It is extremely vital to diagnose VAP accurately and rapidly and to reduce mortality by initiating appropriate treatment in these patinsts.

Material and Methods

The present study was carried out in a tertiary care teaching hospital at Ahmedabad. Patients above the age of 15 years, receiving MV for more than 48 hours at ICU with clinical suspicion of VAP were evaluated. All patients had no evidence of pneumonia on admission. Details, like, age, gender, admission diagnosis, indication for MV, details of clinical examination and laboratory investigations (haemogram, serum biochemistry) and radiological investigations (chest radiograph) were noted for all the patients. Modified baseline clinical pulmonary infection score (CPIS) was calculated for each patient. Arterial blood gas analysis was done, whenever possible.

Patients were monitored for the development of VAP. Clinically suspected pneumonia was defined as the presence of new and/or progressive infiltrate on chest radiography with no other obvious cause and the presence of any two of the following: (1) temperature ≥ 38 °C or ≤ 36 °C, (2) white blood cell count $\geq 11 \times 10^9$ /L or $\geq 4 \times 10^9$ /L and (3) purulent tracheal secretions or change in the character of tracheal secretions.[6]

Fiberoptic bronchoscopy was performed in all the patients with clinically suspected pneumonia to diagnose VAP. Bronchoalveolar lavage culture with a threshold value of 10^4 cfu/mL or more was considered positive and included in the study.[7] Out of 94 clinically suspected cases of VAP, BAL culture was positive in 50 (53%) cases.

The enrolled patients were followed up until they were successfully treated and discharged from the hospital or until death. Endotracheal intubation was done to initiate MV and tracheostomy was done if a patient required MV for prolonged period. The patients were managed through invasive ventilators (SERVO Ventilator 900c [Siemens-Elema, Sweden]). The ventilators in our institution are equipped to provide MV by different modes. Respiratory physiotherapy was given by a trained physiotherapist during the routine hours. The patients were weaned off from MV as per standardised weaning protocols.[8]

Statistical Analysis

Data entry and data analysis was done by using MS Excel 10 and EPI info 7.2 version. The tests used for analysis were percentage (%) and Chi square test.

Results

In the present study, 50 patients of VAP were included. The age of patients ranged from 16 to 72 years; 31 (62%) in the age group 41-60 years, 10 (20%) more than 60 years and 3 (6%) were below 20 years. Out of 50 patients, 37 (74%) were males. Neurological conditions including Guillain-Barre syndrome, cerebrovascular accident, meningitis, snake-bite were the most common conditions for MV. Tropical issues like, fulminant tetanus, organophosphurus poisoning and cerebral malaria were the other common indications for MV. In our ICU, only 8 (16%) patients required MV due to respiratory disorders including acute exacerbations of chronic obstructive pulmonary disease, miliary tuberculosis and bronchial asthma.

The duration of MV at the time of onset of VAP ranged from 3 days to 38 days. VAP developed within 15 days of the initiation of MV in 38 (76%) patients, between 16 to 38 days in 12 (24%) patients. The onset of VAP was most common during the first two weeks of initiation of MV (Table 1).

Purulent tracheal secretions were observed in 35 (70%) patients, whereas fever was present in 33 (66%) patients. Leucocytosis was observed in 38 (64%) and leucopaenia in 2 (40%) patients. Crepitations or dullness to percussion on chest examination was present in 10 (20%) patients and hypothermia in only one patient.

Table 1. Incidnece of ventilator-associated pneumonia with relation to number of days of mechanical ventilation (MV).

Number of Days of MV	Number of Patients (%)
3 – 5	7 (14)
6 – 10	20 (40)
11 – 15	11 (22)
16 – 20	6 (12)
21 – 25	3 (6)
26 – 30	1 (2)
31 – 35	1 (2)
≥ 36	1 (2)
Total	**50 (100)**

The clinical pulmonary infection score (CPIS) was based on six variables including temperature, leucocyte count, tracheal secretions, chest radiograph infiltrates, oxygenation (PaO_2 / FIO_2 ratio) and microbiological culture of the tracheal aspirates. The modified baseline CPIS was calculated using the first five variables. Modified baseline CPIS ≥6 was present in 43 (86%) patients and in 7 (14%) patients CPIS was <6. Lowest modified baseline CPIS was 4 found in 3 (6%) patients and highest was 9 found in two (4%) patients (Table 2).

Table 2. Modified baseline clinical pulmonary infection score (CPIS) in patients with ventilator-associated pneumonia.

Modified Baseline CPIS	Number of Patients (%)
4	3 (6)
5	4 (8)
6	23 (46)
7	13 (26)
8	5 (10)
9	2 (4)
10	0 (0)
Total	**50 (100)**

Microbiological profile of isolated organisms in patients with VAP is presented in table 3. Among Gram-negative bacilli, *Pseudomonas aeruginosa* (13 [23.2%]), *Haemophilus influenzae* (6 [10.7%]) and *Enterobacter* (5 [8.9%]) were the leading aetiological micro-organisms. Bacilli isolated were *Escherichia coli, Klebsiella pneumoniae, Serratia, Proteus* and *Acinetobacter.* Among gram-positive cocci, *Staphylococcus aureus* (14 [25%]) was the leading aetiological micro-organism and *Streptococcus pneumoniae* was isolated in two (3.6%) cases. Of these, monomicrobial aetiology was observed in 44/50 (88%) patients and polymicrobial aetiology in 6/50 (12%) patients (Table 3). Out of 16 cases of early onset VAP, *Haemophilus influenza,* Methicillin-sensitive *staphylococcus aureus, Streptococcus pneumoniae* were the leading aetiological agents (Table 3). Out of 40 micro-organisms isolated in late onset VAP, *Pseudomonas, Methicillin-resistant staphylococcus aureus, Enterobacter, Klebsiella pneumoniae* were the leading aetiological agents (Table 3).

In cases of early-onset VAP, four patients died whereas out of 34 patients of late-onset VAP, 17 patients died. Mortality rate in late-onset VAP (50%) was significantly higher than that of early-onset VAP (25%).

Appropriate treatment is defined as administration of antibiotic drugs that are active against all lower respiratory isolates or those isolated in significant concentration by invasive methods. Out of 32 appropriately treated patients, 10 died, whereas 11 patients died from 18 inappropriately treated patients. Mortality in inappropriately treated patients (61.1%) was significantly higher than that of appropriately treated patients (31.3%).

Discussion

Ventilator-associated pneumonia is a common complication in mechanically ventilated patients. Due to large disease burden and morbidity and mortality attributed to VAP, there is great interest in accurately diagnosing, treating, and preventing this complication. The bronchoscopy methods, like, BAL and protected specimen brush (PSB) are well standardised and widely accepted invasive diagnostic techniques for identifying the aetiological pathogen for VAP.

Table 3. Microbiolocal profile of isolated organisms depending on the duration of onset of ventilator-associated pneumonia.

Microorganisms	Number of Organisms Isolated No. (%)	Early-onset VAP No. (%)	Late-onset VAP No. (%)
Gram Negative Bacilli			
Pseudomonas aeruginosa	13 (23.2)	2 (3.6)	11 (19.6)
Escherichia coli	2 (3.6)	0 (0)	2 (3.6)
Klebsiella pneumoniae	3 (5.3)	0 (0)	3 (5.4)
Enterobacter	5 (8.9)	1 (1.8)	4 (7.1)
Serratia	2 (3.6)	0 (0)	2 (3.6)
Protens	2 (3.6)	0 (0)	2 (3.6)
Hemophilus influenzae	6 (10.7)	5 (8.9)	1 (1.8)
Acinetobacter	2 (3.6)	0 (0)	2 (3.6)
Gram Positive Cocci			
MSSA	6 (10.7)	5 (8.9)	1 (1.8)
MRSA	8 (14.3)	0 (0)	8 (14.3)
Streptococcus pneumoniae	2 (3.6)	2 (3.6)	0 (0)
Others*	5 (8.9)	1 (1.8)	4 (7.1)
Total	**56 (100)**	**16 (28.6)**	**40 (71.4)**

*(1) Coagulase negative *Staphylococcus aureus*, (2) *Citrobacter*, (3) *Stenotrophomonas maltophilia*, (4) *Streptococcus* species, (5) *Moraxella catarrhalis*

Definition of abbreviations: VAP=Ventilator-associaed pneumonia, MSSA=Methicillin-sensitive *staphylococcus aureus*, MRSA=Methicillin-resistant *staphylococcus aureus*

Incidence of VAP is defined as number of VAP cases per 100 ventilated patients which depends on hospital setting, diagnostic criteria used to confirm pneumonia, mean duration of MV and underlying medical conditions. In the present study, the incidence of VAP is 21% which is in contrast with other studies.[9-13] In all these studies BAL or PSB was used as diagnostic criteria for VAP. However, the high incidence of VAP in the study by Kerver *et al*[14] (67%) is due to the use of only clinical criteria to diagnose VAP.

In the present study, VAP developed within 15 days of initiation of MV in 75% cases, in contrast with an earlier study by Emad H. Ibrahim *et al.*[15] However, another study[16] reported that 89.3% of their study patients developed VAP within 15 days of initiation of MV. It is evident that the onset of VAP is most common during the first 15 days of initiation of MV.

There were similar results with repect to other variables, like purulent tracheal secretions, fever, leucocytosis, rales or dullness to percussion on chest examination, leucopaenia and hypothermia as compared to the study by Camargo *et al*.[17]

In a mechanically ventilated patient, if CPIS is ≥6, the probability of VAP is high. In the present study, we observed CPIS ≥6 in 43 (86%) of patients, which is in contrast with other studies.[18-20] However, if CPIS is <6, it does not rule out VAP, as in the present study 7 (14%) patients had CPIS <6 who developed VAP. Therefore, routine monitoring of CPIS of mechanically ventilated patients may be done for suspicion of VAP.

The total number of isolated organisms is more than the number of patients because some patients had more than one isolate. Among Gram-negative bacilli, *Pseudomonas* (23.2%), *Haemophilus influenzae* (10.7%), *Enterobacter* (8.9%) were the leading aetiological agents. Among Gram-positive cocci, *Staphylococcus aureus* (25%) was the leading aetiological agent. The micro-organisms profile observed in the present study is comparable with other studies.[21-23]

Pseudomonas aeruginosa and *Staphylococcus aureus* were observed to be the major antibiotic resistant pathogens. A total of 56 micro-organisms were isolated in 50 cases of VAP. Polymicrobial VAP was present in six (12%) patients in the present study, in contrast with other studies.[22,24] However, Fagon *et al*[23] reported polymicrobial VAP in 27.8% of their study patients. Polymicrobial infection is usually a combination of aerobic Gram-negative bacilli along with *Staphylococcus aureus* or other Gram-positive cocci. Presence of polymicrobial VAP requires combination of antibiotics to cover all the micro-organisms isolated.

Ventilator-associated pneumonia increases mortality in mechanically ventilated patients.[9-13] Mortality in inappropriately treated patients is significantly higher than that of appropriately treated patients. Overall mortality observed in the present study was 61.1% in inappropriately treated patients and 31.3% in appropriately treated patients. However, in other studies,[25-27] mortality in inappropriately treated patients was reported to be 92%, 57%, 82%, 63%, respectively. It is extremely imperative that treatment of VAP must be started promptly with adequate and appropriate antibiotics to reduce morbidity and mortality.

Mortality is high in late onset VAP (VAP developing >7 days after initiation of MV) and low in early onset VAP (VAP developing ≤7 days after initiation of MV).[30] The difference of mortality in early- and late-onset VAP may be due to difference of micro-organisms commonly isolated in early- and late-onset VAP and their susceptibility to antibiotics. In the present study, mortality in early and late onset VAP was 25% and 50%, respectively, which is in contrast with other sutides.[10,31]

Conclusions

Ventilator-associated pneumonia (VAP) is a common complication in mechanically ventilated patients. All necessary preventive measures must be taken to reduce the incidence of VAP in intensive care unit. Due to large disease burden and morbidity and mortality attributed to VAP, there is great interest in accurately diagnosing, treating, and preventing this complication. VAP increases duration of hospital stay, morbidity and mortality in mechanically ventilated patients; if not treated appropriately early.

References

1. Pennington JE. Nosocomial respiratory infection. In: Mandell GL, Douglas RG Jr, Bennet JE, editors *Principles and Practice of Infectious Diseases*. St. Louis, MO: Churchill Livingstone; 1990: p. 2199–2205.
2. Campbell GD, Nieder MS, Broughton WA, *et al*; American Thoracic Society. Hospital acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy, and preventive strategies. *Am J Respir Crit Care Med* 1995;153:1711-25.
3. Ioanas M, Ferrer R, Angrill J, Ferrer M, Torres A. Microbial investigations in ventilator associated pneumonia. *Eur Respir J* 2001;17:791–801.
4. Morehead RS, Pinto SJ. Ventilator associated pneumonia. *Arch Intern Med* 2000;160:1926–36.
5. Corley DE, Kirtland SH, Winterbauer RH, Hammar SP, Dail DH, Bauermeister DE, *et al*. Reproducibility of the histologic diagnosis of pneumonia among a panel of four pathologist. *Chest* 1997;112:458–65.
6. Fabregas N, Ewig S, Torres A, El-Ebiary M, Ramirez J, de La Bellacasa JP, *et al*. Clinical diagnosis of ventilator associated pneumonia revisited: comparative validation using immediate post-mortem lung biopsies. *Thorax* 1999;54:867–73.
7. Chastre J, Fagon JY, Bornet-Lecso M, Calvat S, Dombret MC, al Khani R, *et al*. Evaluation of bronchoscopic techniques for the diagnosis of nosocomial pneumonia. *Am J Respir Crit Care Med* 1995;152:231–40.
8. Wawrzyniak T, Stoen J for Fairview Southdale Hospital, France. Protocol Development, application and use. 2000; *Available at URL*: http://www.ventworld.com/resources/contrib/wawrzyn.pdf.
9. Torres A, Aznar R, Gatell JM, Jimenez P, Gonzalez J, Ferrer A, *et al*. Incidence, risk, and prognosis factors of nosocomial pneumonia in mechanically ventilated patients. *Am Rev Respir Dis* 1990;142:523–8.
10. Timsit JF, Chevret S, Valcke J, Misset B, Renaud B, Goldstein FW, *et al*. Mortality of nosocomial pneumonia in ventilated patients: influence of diagnostic tools. *Am J Respir Crit Care Med* 1996;154:116–23.
11. Fagon JY, Chastre J, Vuagnat A, Trouillet JL, Novara A, Gibert C. Nosocomial pneumonia and mortality among patients in intensive care units. *JAMA* 1996;275:866–9.

12. Tejada Artigas A, Bello Dronda S, Chacon Valles E, Munoz Marco J, Villuendas Uson MC, Figueras P, *et al*. Risk factors for nosocomial pneumonia in critically ill trauma patients. *Crit Care Med* 2001;29:304–9.
13. Cook DJ, Walter SD, Cook RJ, Griffith LE, Guyatt GH, Leasa D, *et al*. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. *Ann Intern Med* 1998;129:433–40.
14. Kerver AJ, Rommes JH, Mevissen-Verhage EA, Hulstaert PF, Vos A, Verhoef J, *et al*. Colonization and infection in surgical intensive care patients: a prospective study. *Int Care Med* 1987;13:347–51.
15. Ibrahim EH, Tracy L, Hill C, Fraser VJ, Kollef MH. The occurrence of VAP in a community hospital: risk factors and clinical outcome. *Chest* 2001;120:551–61.
16. Apostolopoulou E, Bakakos P, Katostaras T, Gregorakos L. Incidence and risk factors for VAP in 4 multidisciplinary ICU in Athens, Greece. *Respir Care* 2003;48:681–8.
17. Camargo LF, De Marco FV, Barbas CS, Hoelz C, Bueno MA, Rodrigues M Jr, *et al*. Ventilator associated pneumonia: comparison between quantitative and qualitative culture of tracheal aspiration. *Crit Care* 2004;8:R422–R430.
18. Schurink CAM, Nieuwenhoven CAV, Jacobs JA, Rozenberg-Arska M, Joore HCA, Buskens E, *et al*. Clinical pulmonary infection score for ventilator-associated pneumonia: accuracy and inter-observer variability. *Int Care Med* 2004;30:217–24.
19. Luyt CE, Chastre J, Fagon JY. Value of CPIS for the identification and management of VAP. *Inte Care Med* 2004;30:844–52.
20. Fartoukh M, Maitre B, Honoré S, Cerf C, Zahar JR, Brun-Buisson C, *et al*. Diagnosing pneumonia during mechanical ventilation, the clinical pulmonary infection score revisited. *Am J Respir Crit Care Med* 2003;168;173–9.
21. Fowler RA, Flavin KE, Barr J, Weinacker AB, Parsonnet J, Gould MK. Variability in antibiotic prescribing patterns and outcomes in patients with clinically suspected ventilator-associated pneumonia. *Chest* 2003;123:835–44.
22. Sirvent JM, Vidour L, Gonzalez S, Castro P, de Batlle J, Castro A, *et al*. Microscopic examination of intracellular organisms in protected bronchoalveolar mini-lavage fluid for the diagnosis of ventilator associated pneumonia. *Chest* 2003;123:518–23.
23. Fagon JY, Chastre J, Wolff M, Gervais C, Parer-Aubas S, Stéphan F, *et al*. Invasive and non-invasive strategies for management of suspected ventilator-associated pneumonia: a randomized trial. *Ann Intern Med* 2000;132:621–30.
24. Singhal R, Mohanty S, Sood S, Das BK, Kapil A. Profile of bacterial isolated from patients with VAP in tertiary care hospital in India. *Indian J Med Res* 2005;121:63–64.
25. Celis R, Torres A, Gatell JM, Almela M, Rodríguez-Roisin R, Agustí-Vidal A. Nosocomial pneumonia: a multivariate analysis of risk and prognosis. *Chest* 1988;93:318–24.
26. Kollef MH, Ward S. The influence of mini-BAL culture on patients outcome: implications for the antibiotic management of ventilator-associated pneumonia. *Chest* 1998;113:412–20.
27. Luna CM, Vujacich P, Niederman MS, Vay C, Gherardi C, Matera J, *et al*. Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia. *Chest* 1997;111:676–85.
28. Rello J, Gallego M, Mariscal D, Soñora R, Valles J. The value of routine microbial investigation in ventilator-associated pneumonia. *Am J Respir Crit Care Med* 1997;156:196–200.
29. Ruiz M, Torres A, Ewig S, Marcos MA, Alcón A, Lledó R, *et al.* Non invasive versus invasive microbial investigation in VAP. Evaluation of outcome. *Am J Respir Crit Care Med* 2000;162:119–25.
30. Vallés J, Pobo A, García-Esquirol O, Mariscal D, Real J, Fernández R. Excess ICU mortality attributable to ventilator-associated pneumonia: the role of early vs late onset. *Intensive Care Med* 2007;33:1363–8.
31. Heyland DK, Cook DJ, Griffith L, Keenan SP, Brun-Buisson C. The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient. The Canadian Critical Trials Group. *Am J Respir Crit Care Med* 1999;159:1249–56.