ejpmr, 2017,4(7), 566-570

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

A PROSPECTIVE MICROBIOLOGICAL STUDY FOR VENTILATOR ASSOCIATED PNEUMONIA IN A TERTIARY CARE HOSPITAL

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Article Received on 05/05/2017 **Article Revised on 24/05/2017** **Article Accepted on 14/06/2017**

ABSTRACT

This study was carried out to isolate and to identify the bacterial etiological agents associated with ventilator associated pneumonia (VAP) and to perform antimicrobial susceptibility tests of these bacterial isolates and to recommend proper use of antibiotics to reduce the mortality, morbidity and costs to the patients or hospitals resulting from VAP. 212 bronchoalveolar lavage (BAL) fluid from intubated and mechanically ventilated ICU patients and later 73 patients, out of these who developed VAP, were taken as samples. Bacteriological studies were performed on these samples. Among the bacterial causative agents Klebsiella, Pseudomonas, S.aureus and E.coli were found to be the commonest in patients with VAP. The most sensitive antimicrobial agents against the Gram -ve bacteria are piperacillin-tazobactam, meropenem, ceftazidime, ceftriaxone-tazobactam, kanamycin and tobramycin. The Gram +ve cocci were found to be most sensitive to meropenem, linezolid, piperacillin-tezobactam and levofloxacin. The selection of initial antimicrobial therapy, before the present microbiological report is available, is based predominantly emperically on previous pattern of microbiological profile and their sensitivity pattern to different antimicrobial agents which vary from ICU to ICU. But the earliest information, provided by the present microbiological examination of BAL fluid from patients suffering from VAP, will provide the earliest and appropriate antimicrobial therapy in the settings of life threatening infections in ICU.

KEYWORDS: Ventilator associated pneumonia, Bronchoalveolar lavage, Kirby-Bauer, MRSA, ESBL, Klebsiella, Pseudomonas, E.coli.

INTRODUCTION

Ventilator associated pneumonia (VAP) is a pneumonia that is developed in mechanically ventilated patients after 48 hours of intubation and starting invasive mechanical ventilation, without any suggestive signs and symptomps of pneumonia at the starting of mechanical ventilation. It also includes pneumonia developing 48 hours after intubation, even if extubation is done[1,2] It is one of the most common nosocomial infection, occuring in intubated and mechanically ventilated patients in ICU. It continues to complicate the course of illness of patients receiving continuous invasive mechanical ventilation. VAP is associated with higher rate of mortality, morbidity and costs to the patients and hospital.[3] The mortality and morbidity rate from VAP ranges from 24% to 50% and may reach to 76% in some specific settings or when lung infections are caused by high risk pathogens.[4] The bacterial etiological agents for VAP widely differ from ICU to ICU according to the population of patients in an ICU, duration of hospital stay and prior antibiotic therapy. Sometimes VAP becomes the major cause of morbidity and mortality among critically ill patients.[5,6] So, the prompt delivery of appropriate antibiotics according to microbiological study seems to be the only intervention that alters the outcome of ICU patients. The aim of this prospective study is to know the bacterial agents and their sensitivity-resistance pattern to different antibiotics and to reduce the mortality, morbidity and costs of patients those developed VAP in ICU of Sir T. Hospital at Bhavnagar, in Gujarat.

MATERIAL AND METHODS

This study was conducted at the Microbiological Department of Sir T. Hospital of Government Medical College, at Bhavnagar in Gujarat. The study population has included the patients admitted in ICU of this hospital and those who were intubated and mechanically ventilated for many serious illness. The patients those were ventilated for more than 48 hours and developed pneumonia were included in this study. Data collection at the time of admission include the admission date in ICU, age and sex of the patients, primary diagnosis of the illness, indication of ventilation, etc. Other datas that were collected include the details of antibiotic therapy, duration of stay in ICU and different vital parameters of

patients. The others clinical criteria for diagnosis of VAP that were included were modified clinical pulmonary infection score (CPIS) >6 [Table-1] and microbiological criteria included a positive Gram stain (>10 polymorphonucler cells / low power field and >1 bacteria/ oil immersion field with or without the presence of intracellular bacteria) and quantitative culture of BAL fluid showing > 10^5 CFU/ml.[8.9.10] Table-1.

Based on the clinical and microbiological criteria, 73 patients were diagnosed as developing VAP. The organisms isolated by quantitative culture method of BAL fluid were identified by standard microbiological technique.[11] The sensitivity and resistance pattern of the microbiological isolates to the routinely used antimicrobial agents were determined by Kirby-Bauer disk diffusion method.[12] The oxacillin screen agar test[13] and the combination disk method[14] using cefotoxime and ceftazidime alone or in combination with clavulinic acid were used to detect Methecillin.

Table --1: Modified Clinical Pulmonary Infection Score (CPIS)

CPIS points	0	1	2
Temperature(^{0}C)	>36.5 but <38.4	>38.5 but <38.9	>39 or <36
Leucocyte counts(per cu. M)	4000-11000	<4000 or >11000	<4000 or >11000 and band forms>500
Tracheal secretions	Rare	Abundant	Abundant +Purulant
PaO_2/FiO_2 mm.Hg	>240 or ARDS	----	------
Chest X-ray	No infiltrate	Diffuse infiltrate	<240 and no ARDS
Culture of BAL fluid	No growth or light growth	Moderate to heavy growth	Moderate or heavy growth +Same bacteria in Gram stain

resistant staphylococcus aureus (MRSA) and extended spectrum beta lactamase (ESBL) producing members of the enterobacteriaceae family. The VAP pathogens, such as the specieses of the genus of Pseudomonas, Acinetobacter and Enteric Gram -ve bacilli producing ESBL and Gram +ve MRSA were defined as multi-drug resistant (MDR) pathogens.[15]

The statistical analysis was carried out using the Chi-square test and the level of significance was set at $P < 0.05$.

RESULT

Out of the total 212 patients, who were on ventilator therapy and were selected for study, 147 patients were in the adult age group and 65 patients were in the pediatric age group. Out of these 212 patients, 73 patients had fulfilled the criteria for the diagnosis of VAP and the growth obtained by culture, had fulfilled the cut-off or threshold value of 10^5 CFU/ml, showing an overall incidence rate of 34.4% (73 cases out of 212 cases).

In pediatric category, out of 65 patients 23 (31.5% of 73) patients and in adult category, out of 147 patients 50 (68.4% of 73) patients, total 23+50=73 patients, had developed VAP. In pediatric category the number of neonates are 6 (40% out of 15neonates) and the number of infants were 10 (32.2% out of 31 infants) those had developed VAP. Males are accounted for 41 (56.1%) and females are accounted for 32 (43.8%) cases. Table-2.

Table--2: Age and sex distribution among VAP patients

Age group	Total patients ventilated	No. Of patients developed VAP	Incidence rate	Male	Female
0-1 months	15	6	40%	4	2
1months-1year	31	10	32.2%	3	7
1yrs-18yrs	19	7	36.8%	5	2
18yrs-65yrs	126	41	32.5%	26	15
>65yrs	21	9	42.8%	6	3
Total	212	73		44	29

Statistical analysis reveled that the duration of mechanical ventilation, the type of MDR pathogens and the intrinsic illness for which the patients were intubated and mechanically ventilated were the significant risk factors for developing VAP. Administration of prior antimicrobial agents is also a significant risk factor for developing VAP, particularly by multi-drug resistant (MDR) pathogens.

A total of 73 bacterial isolates were obtained from BAL fluids of VAP patients. The commonest bacterial isolates were Gram -ve bacilli and its number were 55 (75.3% of 73 bacterial isolates). Within these Gram -ve bacilli, Klebsiella were accounted for 23 (31.5% of 73 bacterial isolates). It was followed by Pseudomonas 19 (26%), E.coli 8 (10.9%) and Acinetobacter 5 (6.8%). Table-3.

Among the bacterial isolates from BAL fluid, the number of Gram +ve cocci accounts for 18 (24.6% of 73 bacterial isolates). Within these Gram +ve cocci, the commonest organism was Staphylococcus aureus and it accounts for 10 (13.6% of 73 bacterial isolates). It is followed by Staphylococcus epidermidis 5 (6.8%) and Enterococci 3 (4.1%).

According to the result of sensitivity of bacterial isolates, the Klebsiella was found to be most sensitive to piperacillin-tazobactam, meropenem, ceftazidime, ceftriaxone-tazobactam, kanamycin and tobramycin in decending order. Pseudomonas was found to be most sensitive to meropenem, aztreonam, piperacillin-tazobactam, levofloxacin and tobramycin. E.coli was most sensitive to ceftazidime, ceftriaxone-tazobactam, and levofloxacin. Acinetobacter was most sensitive to piperacillin-tazobactam, ceftriaxone-tazobactam, meropenem and tobramycin. Among the Gram +ve cocci, S.aureus was most sensitive to teicoplanin, linezolid, piperacillin-tazobactam and levofloxacin.

Table--3: Bacterial isolates from BAL fluid in VAP patients

Name of organism isolated	Number	Percentage
Klebsiella	23	31.5%
Pseudomonas	19	26%
E.coli	8	10.9%
Acinetobacter	5	6.8%
Total Gram -ve bacilli isolated	55	75.3%
S.aureus	10	13.6%
CONS	5	6.8%
Enterococcus	3	4.1%
Total Gram +ve cocci isolated	18	24.6%

In our study, 26 (35.6%) of the 73 bacterial isolates from VAP patients were found to be are of MDR type. These include 9 (39.1%) out of 23 isolated Klebsiella are of ESBL producing and 4 (50%) out of 8 isolated E.coli are of ESBL producing. Out of 19 Pseudomonas isolates, 11 (57.8%) are of multi drug resistant (MDR) and out of 5 Acinetobacter, 2 (40%) are of MDR type.

In our study, a total of 23 out of 73 patients with VAP were expired, accounting for a mortality rate of 31.5%(23 out of 73). Among 6 neonates, those developed VAP, 3 (50%) were expired.

Mortality incidences of different age group are shown in the table. Table-4.

Table-4: Mortality rate in VAP patients.

Age	Number of VAP patients	No of patients expired	Incidences rate
0-1month	6	3	50% of 6 neonates
1months--1yrs	10	3	30% of 10 infants
1yrs--18yrs	7	2	28.5% of 7 children
18yrs--65yrs	41	10	24.3% of 41 adults
>65yrs	9	5	55.5% of 9 geriatrics
Total	73	23	

DISCUSSION

Among the intubated and mechanically ventilated ICU patients, the ventilator associated pneumonia is an important form of nosocomial infection. The overall incidence of VAP in this study is 34.4%. This is marginally lower than the incidence of 37%, reported by Gadani et al[15] in a study of 37 patients on ventilator therapy. This could be due to the fact that our study included the patients mainly of adult age group. The incidence of VAP in our study is also lower than another study done by R. M.Saldanha Dominic et al. A probable reason for the higher incidence of VAP in the study by Dominic could be that neonates and infants constituted the majority of cases of VAP. The immune system and the immune mechanisms are not well developed in neonates and infants, thereby placing them at a higher risk of infections and mortality.

In our study, the duration of mechanical ventilation and the illness for which the mechanical ventilation was started, these two determinants, were statistically significant risk factors for development of VAP.[16] The reduction of the duration of mechanical ventilation significantly decreases the incidence of VAP and with it the rate of morbidity, mortality, hospital stay and the cost to the patients. This reduction of the duration of mechanical ventilation may be due to the improvement of clinical illness for which the patient was put on mechanical ventilation. The reduction of duration of mechanical ventilation also subsequently reduces the risk of exposure of patients to MDR pathogens.

A proper weaning protocol is also important for the reduction of the incidence of VAP, by reducing the the duration of mechanical ventilation. Improper weaning may lead toreintubation and further prolonged mechanical ventilation and thus a vicious cycle may start. Once daily trial of spontaneous breathing and a prolonged period of rest may be the best effective method of weaning. It recondition the respiratory muscles that may have been weakened during continuous mechanical ventilations.[17,18]

Increased duration of mechanical ventilation is also related with prior antibiotic therapy and statistically significant risk factor for development of VAP. The use of antibiotics as a prophylactic measure against VAP is not recommended[19] as prior exposure to antibiotics is a significant risk factor for colonization and infections with nosocomial MDR pathogens. This is also observed in other studies.[1,20,21] The rational use of appropriate antibiotics may reduce the patients colonization by MDR pathogens and subsequent development of VAP.

The majority of bacterial isolates in our study were Gram -ve bacilli and its number was 55(75.3%). Among these the specieses of Klebsiella, Pseudomonas, E.coli and Acinetobacter genus were accounted for 23(31.5%), 19(26.02%), 8(10.9%), 5(6.8%), respectively. The S. aureus was predominant among the Gram + ve isolates. In our study, Pseudomonas is the second most common bacterial isolates after Klebsiella. It is an ubiquitous organism, present everywhere in the environment. Pseudomonas infection occurs when there is compromise of host defense, mucosal trauma, antibody mediated suppression of normal flora of body, etc. It is commonly identified in respiratory therapy equipments, disinfectants, sinks, etc. Because of its hardiness, ubiquitiousness and easy ability to capitalize on breakdown of human antimicrobial defense, it is a common nosocomial pathogen. The result of our study with reference to the etiology of VAP shows that tracheal intubation is associated with increased frequency of Gram negative bacterial colonization of upper and lower respiratory tract. This is followed by rapid growth of these Gram negative bacteria and development of pneumonia.

Several studies also have reported that more than 60% of nosocomial pneumonia are caused by aerobic Gram negative bacilli. Klebsiella, Pseudomonas, E.coli, Acinetobacter and other Gram negative bacterial species adhere five times better to respiratory epithelial cells of severely ill patients than to the epithelial cells of other normal sites. Similar level of increased adherence also has been demonstrated for respiratory epithelial cells of critically ill patients.[22] These Gram negative organisms also reflect the organisms with same sensitivity-resistance pattern in other studies and their ability to survive in the hospital environment.

Multi-drug resistant (MDR) bacteria have been defined as bacteria which are resistant to one agent in three or more categories of antibiotics.[24] It is mainly the gram-negative rods that survive in myriad of enviorment such as aquatic and terrestrial and easily acquaired resistant to multiple antimicrobial agents. The inherent antimicrobial resistance mechanisms include lower outer membrane permiability, increased expression of efflux pumps of different specificity to different antimicrobial agents and presence of Amp C beta-lactamase enzyme.

In our study, 26 isolates (35.6%) from VAP patients were found to be MDR pathogens. These include Pseudomonas, Acinetobacter and MRSA. Inaddition, ESBL producing strains of Klebsiella and E.coli were also isolated. Though our findings are significantly lower than other studies[23], the etiology of VAP by MDR pathogens remains the same. This reinforces the need for vigilance in taking preventive measures against VAP.

The mortality rate resulting from ventilator associated pneumonia in this study is 31.5% with neonates and elderly above 65 years accounting for a majority of deaths. The poorly developed immune system in neonates and waning of immune defense mechanisms in elderly may explain the reason for poor recovery from pneumonia developed or associated with mechanical ventilation.

CONCLUSION

Strict aseptic measures are required during intubation and starting of invasive mechanical ventilation for all patients those needs it in ICU. This is followed by continuous high grade vigilance and monitoring during the period of ventilation to detect and to prevent the development of ventilator associated pneumonia. For that, monitoring of body temperature, blood leucocyte count, chest radiograph, etc. should be performed routinely according to the ICU protocol or as and when necessary. For microbiological diagnosis during earliest period of developing pneumonia BAL fluid should be send for culture and sensitivity. Antibiotic if is used from before, should be changed according to sensitivity reports. It should also be kept in mind that VAP can be caused by MDR pathogens. Beside the use of antibiotics according to the report of sensitivity, addition of aseptic measures while handling a mechanically ventilated patients and adequate preventive measures to minimize the risk factors, will definitely improve the outcome of a mechanically ventilated patients by preventing the development of ventilator associated pneumonia. If, once VAP is developed, then it is very difficult to treat and mortality goes up.

ACKNOWLEDGMENT

The author acknowledges all the faculties and the stuffs of the Department of Microbiology and the Department of Anesthesiology of Government Medical College, Bhavnagar, Gujarat. for providing the necessary inputs during the conduct of this study. The author also

acknowledges all the brothers and sisters of ICU of Sir T. Hospital of Government Medical College of Bhavnagar for their kind co-operations.

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