STUDY OF MICROBIOLOGICAL SURVEILLANCE AND ANTIBIOTIC STEWARDSHIP IN VENTILATOR ASSOCIATED PNEUMONIA

Ajay Kumar Mishra[1], Davendra Kumar[2], Mehboob Subhani Siddiqui[3], Jyoti Gurang Mannari[4], Suman Praveen Singh[5], Sneha Chaudhary[6]

[1]Associate Professor, Department of Medicine, Era's Lucknow Medical College, Lucknow, Uttar Pradesh.
[2]Associate Professor, Department of Medicine, Era's Lucknow Medical College, Lucknow, Uttar Pradesh.
[3]Professor, Department of Medicine, Era's Lucknow Medical College, Lucknow, Uttar Pradesh.
[4]Professor, Department of Medicine, Pramukhswami Medical College, Karamsad, Gujarat.
[5]Professor, Department of Microbiology, Pramukhswami Medical College, Karamsad, Gujarat.
[6]Senior Resident, Department of Medicine, Pramukhswami Medical College, Karamsad, Gujarat.

ABSTRACT

BACKGROUND

Ventilator-Associated Pneumonia (VAP) continues to be a major problem in critically ill patients. The objective of this research was to know the burden of ventilator-associated pneumonia and effectiveness of antibiotic stewardship in Medical Intensive Care Unit (MICU) of our institution.

METHODS

This prospective observational study was carried out for one year at our institution. It included all patients more than 18 years of age admitted to MICU who underwent invasive mechanical ventilation for more than 48 hours. Among these, patients who developed VAP as per the CPIS score were identified. Laboratory results were correlated with the patient's clinical condition and adjunct investigations. The presumptive therapy for treatment of hospital acquired pneumonia was based on surveillance by hospital infection control unit. All patients who received empiric antimicrobial therapy were analysed against bacterial sensitivity.

RESULTS

The VAP rate was 67 cases per 1000 ventilator days. The incidence of early VAP was 47.5% and incidence of late VAP was 52.5%. Gram negative isolates in particular Acinetobacter baumannii were more frequent than the Gram positive isolates in early and late VAP; 95% Acinetobacter baumannii isolates were resistant to Carbapenem and sensitive to only Colistin in 67.6% cases, Colistin and Tigecycline in 24.3% cases and to other antibiotics in 8.1% cases. There were inappropriate empirical antibiotic prescriptions in 80% of instances and required a change of antibiotics after the culture and sensitivity report.

CONCLUSIONS

In conclusion, this work demonstrates the importance of an active surveillance program in multi-drug resistance outbreak recognition in our ICU and review of antimicrobial use to prevent emergence of antibiotic resistance strains and to preserve existing therapeutic option for caring for such infections.

KEYWORDS

Microbiological Surveillance, Antibiotic Stewardship, Ventilator Associated Pneumonia.

HOW TO CITE THIS ARTICLE: Mishra AK, Kumar D, Siddiqui MS, et al. Study of microbiological surveillance and antibiotic stewardship in ventilator associated pneumonia. J. Evolution Med. Dent. Sci. 2016;5(27):1379-1382, DOI: 10.14260/jemds/2016/325

INTRODUCTION

Ventilator-Associated Pneumonia (VAP) continues to be a major problem in critically ill patients. Despite advances in antimicrobial therapy, supportive care and infection control measures, VAP cause considerable morbidity and mortality. Because of the unique combination of critically ill and often immunosuppressed hosts and chronically high antibiotic selective pressures, the Intensive Care Unit (ICU) is an important environment for the emergence of antimicrobial drug resistance and the spread of drug-resistant organisms.[1]

Financial or Other, Competing Interest: None.
Submission 02-03-2016, Peer Review 14-03-2016,
Acceptance 17-03-2016, Published 01-04-2016.
Corresponding Author:
Dr. Ajay Kumar Mishra,
Associate Professor,
Department of Medicine,
Era's Lucknow Medical College,
Lucknow, Uttar Pradesh.
E-mail: dram1967@rediffmail.com
DOI: 10.14260/jemds/2016/325

Antibiotic stewardship involves a multifaceted approach that strives to combat the emergence of resistance, improve clinical outcomes and control costs by improving antimicrobial use.[2] The objective of this research was to know the burden of ventilator-associated pneumonia and effectiveness of antibiotic stewardship in Medical Intensive Care Unit (MICU) of our institution.

SUBJECTS AND METHODS

This study was approved by the Ethics Committee and was performed from 1 February 2014 to 31 January 2015 at our institution, a 550 bedded rural based tertiary care centre. The MICU has 12 beds used exclusively for critically ill medical patients. The staff comprises of three full time intensivist who decides all admissions and treatment in MICU. The study included all patients more than 18 years of age admitted to MICU who underwent invasive mechanical ventilation for more than 48 hours.

Ventilator-Associated Pneumonia (VAP) was defined as pneumonia occurring in a patient within 48 hours after

intubation with an endotracheal or tracheostomy tube and which was not present before admission. The diagnosis of VAP was made by the Clinical Pulmonary Infection Score (CPIS), based on six variables: Temperature, Blood leukocyte count, Volume and Purulence of tracheal secretions, Oxygenation, Pulmonary radiography, Semi-quantitative culture of tracheal aspirate.

Processing of specimens, identification of pathogens and antimicrobial susceptibility testing was carried out as per standard operating protocol. All microorganisms isolated were identified by standard laboratory methods and cultures were semi-quantitatively recorded as CFU/mL. Colonies of $>10^5$ CFU/mL were taken as positive culture growth. Laboratory results were correlated with the patient's clinical condition and adjunct investigations. All patients who received empiric antimicrobial therapy were analysed against bacterial sensitivity.

The antibiotic protocol for treatment of hospital acquired pneumonia was made in cooperation with the Microbiology Department based on surveillance by hospital infection control unit. The presumptive therapy for hospital acquired infection based on surveillance includes Meropenem or piperacillin-tazobactam or Cefepime-tazobactam+amikacin or tobramycin or levofloxacin.

Statistical Analysis Used

T-test was used to compare continuous variable. The Chi-square test was used to compare categorical variables.

RESULTS

During the study, 116 patients admitted in the medical ICU underwent invasive mechanical ventilation. There were 71 (61%) males and 45 (39%) females with a mean age of 53 years. Of the 116 patients we recorded 59 (52%) cases of VAP; the VAP rate was 67 cases per 1000 ventilator days. The incidence of early VAP was 47.5% and incidence of late VAP was 52.5%. The mean duration of ICU stays in patients who developed VAP was 11 days.

Among 59 VAP cases, 45 (76%) had underlying comorbidities. The top three most common comorbidities were diabetes mellitus, chronic kidney disease and ischemic heart disease. The major reasons for intubation were severe sepsis, altered level of consciousness, pulmonary oedema and seizures.

59 cases of VAP yielded a total of 67 positive cultures of which 62 (92%) were Gram negative and 5 (8%) cultured Gram positive organisms. There was no fungal infection reported during the study. Monomicrobial infection was observed in 56 (95%), while polymicrobial infection was observed in 3 (5%) patients of VAP.

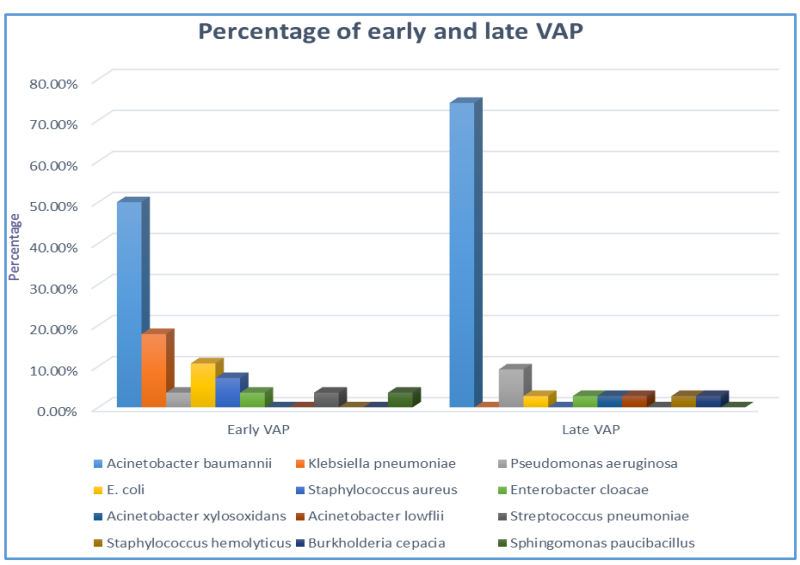
The microorganism profile is shown in Table 1. Gram negative isolates, in particular Acinetobacter baumannii were more frequent than the Gram positive isolates in early and late VAP. (Figure 1) Enterobacteriaceae family, chiefly Klebsiella pneumoniae and Escherichia coli were isolated in 13 (20%) cases. Pseudomonas aeruginosa and Staphylococcus aureus were identified in 5 (8%) and 3(5%) patients, respectively. Among the Acinetobacter family, Acinetobacter baumannii (A baumannii) was the most common organism isolated in 37 (94%) cases; 35 (95%) A baumannii isolates were resistant to carbapenem and sensitive to Colistin in 67.6% cases, Colistin and Tigecycline in 24.3% cases and to other antibiotics in 8.1% cases (Table 2).

There were 62 empirical antibiotic prescriptions; 51 (82%) did not cover the isolated organism and required change based on organism susceptibility. There were 5 (8%) death in 62 patients in whom positive isolates were recovered.

Gram Negative Isolates	(n)
Acinetobacter baumannii	37
Klebsiella pneumoniae	8
Pseudomonas aeruginosa	5
Escherichia coli	5
Enterobacter cloacae	2
Acinetobacter Iwoffii	1
Acinetobacter xylosoxidans	1
Stenotrophomonas maltophilia	1
Sphingomonas paucibacillus	1
Burkholderia cepacia	1

Gram Positive Isolates	(n)
Staphylococcus aureus	3
Staphylococcus haemolyticus	1
Streptococcus pneumoniae	1

Table 1: Microorganisms Profile of Isolates



Antimicrobial Sensitivity (n)%									
Organism (n)	**Meropenem & Imipenem**	**Piperacillin-Tazobactam**	**Ciprofloxacin**	**Amikacin**	**Ceftriaxone**	**Tigecycline**	**Colistin**	**Ampicillin-Sulbactam**	**Cefepime**
Acinetobacter Baumannii (37)	2/37/(5)	2/37/(5)	2/37/(5)	2/37/(5)	0/37/(0)	10/37/(27)	35/37/(27)	0/37/(0)	2/37(5)
Klebsiella Pneumoniae (8)	1/8(12)	1/8(12)	1/8(12)	2/8(25)	0/8(0)	1/8(12)	6/8(75)	0/8(0)	0/89(0)
Pseudomonas Aeruginosa (5)	2/5(40)	0/5(0)	1/5(0)	0/5(0)	0/5(0)	0/59(0)	3/5(60)	0/5(0)	0/5(0)
Escherichia Coli (5)	5/5(100)	2/5(40)	1/5(20)	5/5(100)	0/5(0)	1/5(20)	1/5(20)	0/5(0)	3/5(60)
Acinetobacter SPP(2)	1/5(50)	1/5(50)	1/2(50)	0/2(0)	0/2(0)	1/2(50)	2/2(100)	0/2(0)	1/2(50)
Enterobacter Cloacae (2)	2/2(100)	2/2(100)	2/2(100)	2/2(100)	2/2(100)	0/2(0)	0/2(0)	0/2(0)	2/2(100)
Sphingomonas paucibacillus (1)	0/1(0)	0/1(0)	0/1(0)	1/1(100)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	1/1(100)
Stenotrophomonas maltophilia (1)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	0/1(0)
Burkholderia cepacia (1)	1/1(100)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	0/1(0)	0/1(0)

Antimicrobial Sensitivity (n)%							
Organism (n)	**Ampicillin-Sulbactam**	**Clindamycin**	**Linezolid**	**Cloxacillin**	**Vancomycin**	**Ciprofloxacin**	**Teicoplanin**
Staphylococcus Aureus (3)	0/3(0)	2/3(66)	3/3(100)	2/3(60)	3/3(100)	0/3(0)	3/3(100)
Staphylococcus Haemolyticus (1)	0/1(0)	0/1(0)	1/1(100)	0/1(0)	1/1(100)	0/1(0)	1/1(100)
Streptococcus Pneumoniae (1)	1/1(100)	1/1(100)	1/1(100)	1/1(100)	1/1(100)	1/1(100)	1/1(100)

Table 2: Antimicrobial Sensitivity of Gram-Negative and Gram-Positive Isolates

DISCUSSION

The major observations in the present study were: 1. High occurrence of VAP in our ICU; 2. Gram negative isolates were more frequently than the Gram positive isolates in early and late VAP; 3. High incidence of MDR gram negative organisms, in particular A. baumannii; 4. Inappropriate empirical antibiotic prescriptions in 80% of instances and required change of antibiotics after the culture and sensitivity report.

The high occurrence of VAP in the present study was higher than the studies done earlier.[3],[4],[5],[6],[7],[8] The possible reasons for high trend of VAP are because being a rural based tertiary care centre it has a high admission rate with complex medical problems and understaffed ICU. High nurse to patient ratio (1 to 3/4) in our ICU leads to improper implementation of infection control measures in handling invasive devices/catheters, endotracheal tubes and tracheostomies in our daily practice.

Although the bacterial aetiology can differ between Western and Asian developing countries and even in different wards in a hospital.[9] The present study revealed that gram negative organism was most frequently isolated than gram positive, which correlates well with the studies done in Asian developing countries.[10],[11],[12]

In the present study, we observed a high incidence of MDR gram negative organisms, in particular A. baumannii. A baumannii is a frequent cause of outbreaks in the hospital setting. A growing number of A baumannii strains are MDR and are difficult to control and eradicate.[10] Factors including the duration of mechanical ventilation, length of hospital and ICU stay, previous exposure to antibiotics and local endemic pathogens in a given ICU influence the likelihood of MDR pathogen infection.[13],[14] Most of the A baumannii strain was Carbapenem resistant. Resistance to Carbapenem antimicrobials is nearly always associated with non-susceptibility to other b-lactams, fluoroquinolones and aminoglycosides.[15],[16] A high prevalence of Carbapenem resistant A baumannii strains causing VAP, leave the Colistin as the last therapeutic option to treat infections caused by these organisms.[4],[17],[18] Strategies to minimize the development of resistance such as class restriction, antibiotic cycling and antimicrobial stewardship has been proposed.[2],[19],[20]

Our choice of empirical antibiotic prescription was inappropriate in 80% of instances and required a change of antibiotics after the culture and sensitivity report. Excluding Acinetobacter from the empirical prescription, our choice of empirical antibiotic was correct in 65% of instances. In our institution based on previous surveillance, Colistin was not included for treatment of VAP. In a retrospective study, Rios et al. suggested that in patients previous with a high risk of harbouring MDR non-fermenting Gram-negative bacteria admitted to ICUs, it could be appropriate to begin the empiric initial antimicrobial therapy using Colistin.[21] The current American Thoracic Society/Infectious Diseases Society of America guidelines for hospital acquired, ventilator-associated and healthcare-associated pneumonia recommends considering Colistin as a therapy for patients with VAP attributed to Carbapenem-resistant Acinetobacter spp.[10]

In conclusion, this work demonstrates the importance of an active surveillance program in multidrug resistance outbreak recognition in our ICU and review of antibiotic use to prevent emergence of antibiotic resistance strains and to preserve existing therapeutic option for caring for such infections.

REFERENCES

1. Denys GA, Relich RF. Antibiotic resistance in nosocomial respiratory infections. Clin Lab Med 2014;34(2):257–270.
2. Lawrence KL, Kollef MH. Antimicrobial stewardship in the intensive care unit. Am J Resp Crit Care Med 2009;179(6):434-38.
3. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA 2009;302(21):2323–9.
4. Rosenthal VD, Bijie H, Maki DG, et al. International nosocomial infection control consortium (INICC) report, data summary of 36 countries, for 2004-2009. Am J Infect Control 2012;40(5):396–407.
5. Barbier F, Andremont A, Wolff M, et al. Hospital-acquired pneumonia and ventilator-associated pneumonia: recent advances in epidemiology and management. Curr Opin Pulm Med 2013;19(3):216–28.
6. Thongpiyapoom S, Narong MN, Suwalak N, et al. Device-associated infections and patterns of antimicrobial resistance in a medical-surgical intensive care unit in a university hospital in Thailand. J Med Assoc Thai 2004;87(7):819-21.
7. Petdachai W. Ventilator-associated pneumonia in a newborn intensive care unit. Southeast Asian J Trop Med Public Health 2004;35(3):724-72.
8. Rakshit P, Nagar VS, Deshpande AK. Incidence, clinical outcome and risk stratification of ventilator-associated pneumonia: a prospective cohort study. Indian J Crit Care Med 2005;9(4):211-216.
9. Torres A, Carlet J. Ventilator-associated pneumonia. European task force on ventilator-associated pneumonia. Eur Respir J 2001;17(5):1034-45.
10. Niederman MS, Craven DE, Bonten MJ. American thoracic society and infectious disease society of America (ATS/IDSA): 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.
11. Chawla R. Epidemiology, etiology, and diagnosis of hospital-acquired pneumonia and ventilator-associated pneumonia in Asian countries. Am J Infect Control 2008;36(4):93–100.
12. Apisarnthanarak A, Buppunharun W, Tiengrim S, et al. An overview of antimicrobial susceptibility patterns for gram-negative bacteria from the national antimicrobial resistance surveillance Thailand (NARST) program from 2000 to 2005. J Med Assoc Thai 2009;92(4):91–94.
13. Spellberg B, Blaser M, Guidos RJ, et al. Combating antimicrobial resistance: policy recommendations to save lives. Clin Infect Dis 2011;52(5):397–428.
14. Jones RN. Microbial etiologies of hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia. Clin Infect Dis 2010;51(1):81–7.
15. Gales AC, Jones RN, Forward KR, et al. Emerging importance of multi-drug resistant acinetobacter species and stenotrophomonas maltophilia as pathogens in seriously ill patients: geographic patterns, epidemiological features, and trends in the SENTRY antimicrobial surveillance program (1997–1999). Clin Infect Dis 2001;32(2):104–113.
16. Gales AC, Jones RN, Turnidge J, et al. Characterization of pseudomonas aeruginosa isolates: occurrence rates, antimicrobial susceptibility patterns, and molecular typing in the global SENTRY antimicrobial surveillance program, 1997–1999. Clin Infect Dis 2001;32(2):146–155.
17. Chung DR, Song JH, Kim SH, et al. High prevalence of multidrug-resistant non-fermenters in hospital-acquired pneumonia in Asia. Am J Respir Crit Care Med 2011;184(12):1409–17.
18. Livermore DM. Has the era of untreatable infections arrived? J Antimicrob Chemother 2009;64(1):i29–36.
19. Rahall JJ, Urban C, Horn D, et al. Class restriction of cephalosporin use to control total cephalosporin resistance to nosocomial klebsiella. JAMA 1998;280(14):1233-37.
20. Kollef MH. Is antibiotic cycling the answer to preventing the emergence of bacterial resistance in the intensive care unit? Clin Infect Dis 2006;43(2):S82-S88.
21. Rios FG, Luna CM, Maskin B, et al. Ventilator-associated pneumonia due to colistin susceptible-only microorganisms. Eur Respir J 2007;30(2):307-13.