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Ventilator-associated pneumonia rates and distribution of causative microorganisms in the second stage intensive care unit

Ali Bestami Kepekci

Istanbul Yeni Yuzyil University, Department of Anesthesia, Vocational Health High School, Istanbul, Turkey

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Abstract

Ventilator-associated pneumonia (VAP) is the most important and common infection affecting patients ventilated with mechanical ventilators in intensive care units (ICU). VAP is defined as incubation-free pneumonia at 48-72 hours after endotracheal intubation. This retrospective study included adult patients (> 18 years old) who were hospitalized in our hospital's General ICU between January 2018 and December 2019. According to the culture results, the patients were divided into two groups as VAP developing and non-VAP. The patients were evaluated in terms of causative agents, antibiotic susceptibilities and risk factors. Differences were reflected as significant at $p<0.05$. VAP developed in 43.7% of 87 patients included in the study. The mortality rate in VAP patients was 76.9%(29/38). While the hospitalization days of VAP patients were 34.39 ± 25.55, it was 8.35 ± 5.63 in non-VAP patients. Five different microorganisms causing VAP were detected in ICU. Pseudomonas aeruginosa (25%) was isolated most frequently. It was observed that susceptibility rates and resistance rates of microorganisms isolated to common antibiotics were low. VAP is a condition that affects the morbidity and mortality status of patients followed in ICU. Strategies should be developed to limit exposure to invasive mechanical ventilation, shorten length of ICU stay and rational antibiotic use.

Keywords: Antibiotic resistance, infection control, intensive care units, mortality, patient safety, ventilator-associated pneumonia

Introduction

Patients in intensive care units (ICUs) are often at high risk of death not only because of their critical illness, but also secondary complications such as a hospital infection [1].

Ventilator-associated pneumonia (VAP) is the most important and common infection that affects patients ventilated by a mechanical ventilator in the ICU [2]. VAP is the most common ICU-borne infection and its incidence ranges from 11% to 57.14% [3-5].

VAP is defined as pneumonia that develops 48-72 hours after endotracheal intubation and does not appear to be hatching during admission [6]. VAP poses an important risk for patients hospitalized in ICU. Their prevention and control are crucial. Their prevention ensures improved healthcare quality and minimizes complications.

***Coresponding Author:** Ali Bestami Kepekci, Istanbul Yeni Yuzyil University, Department of Anesthesia, Vocational Health High School, Istanbul, Turkey. E-mail: alibestemi.kepekci@yeniyuzyil.edu.tr

The development of VAP is related to health care and its primary sources are usually secretions secreted from the upper respiratory tract, contaminated materials or reflux of the gastrointestinal tract [7].

Our study aims to determine the incidence of VAP in adult patients in our hospital, to investigate risk factors, associated complications, causative microorganisms and their susceptibility to antibiotics.

Materials and Methods

Study design and patients

This retrospective study included adult patients (> 18 years old) who were hospitalized in Istanbul Meltem Hospital Adult ICU between January 2018 and December 2019. Inclusion criteria were determined to be provided to the invasive mechanical ventilator longer than 48 hours and not to have pneumonia during intubation. The exclusion criteria were defined as having invasive mechanical ventilator support less than 48 hours, having symptoms of pneumonia during intubation and lack of information in their files.

In patients ventilated with a mechanical ventilator, if pneumonia occurred after 48 hours of endotracheal intubation, it was considered VAP. For the diagnosis of VAP, nosocomial pneumonia

criteria were used in line with the "Centers for Disease Control and Prevention (CDC)" recommendations [8].

Endotracheal aspirate was sent for microbiology from patients with fever>38.2 °C, abundant purulent tracheobronchial secretion,WBC count ≥12.000 / mm3 and at least two of the new pulmonary infiltration findings on chest radiographs. Samples were examined by gram staining. Tracheal aspirate culture results were evaluated. Antibiogram studies of patients with any microorganisms detected in their cultures were listed and their sensitivity to antibiotics was determined. Patients with pneumonia during intubation were excluded from the study. The patients included in the study were divided into two groups as patients who did not develop VAP when they were ventilated by mechanical ventilation and patients who developed VAP. Acute Physiologic Assessment and Control Health Evaluation (APACHE II) scoring system and demographic data of all patients were listed.

Age, gender, other comorbidities (diabetes mellitus, chronic obstructive pulmonary disease), clinical diagnosis during hospitalization, duration of intensive care, mechanical ventilation days, mortality status were evaluated to analyze predisposing factors and hospital morbidity.

Statistical analysis

SPSS software version 23(SPSS, Chicago, IL, USA) was used for statistical analyses. The numbers, percentages, means and the standard deviation values were given as the descriptive statistics. Proportions were compared by using the Chi-square test. The level of significance was established by using the student t-test for normally distributed values and Mann Whitney U test for abnormally distributed values. Differences were reflected as significant at $p<0.05$.

Results

In this study, the data of 199 patients hospitalized in ICU were examined. Of these patients, 87 without pneumonia were included in the survey during intubation (Figure 1). The average age of the patients included in the study was (71.59 ± 14.38) years, 50 of them were male and 37 were female. VAP developed in 38 (43.7%) of the patients included in the study.

The demographic characteristics of the patients according to whether VAP develops or not is presented in Table 1. There was no statistically significant difference between the two patient groups in terms of age, gender, primary diseases and APACHE II scores ($p>0.05$).

It was found that 76.9% (29/38) of the patients diagnosed with VAP died during ICU follow-up.

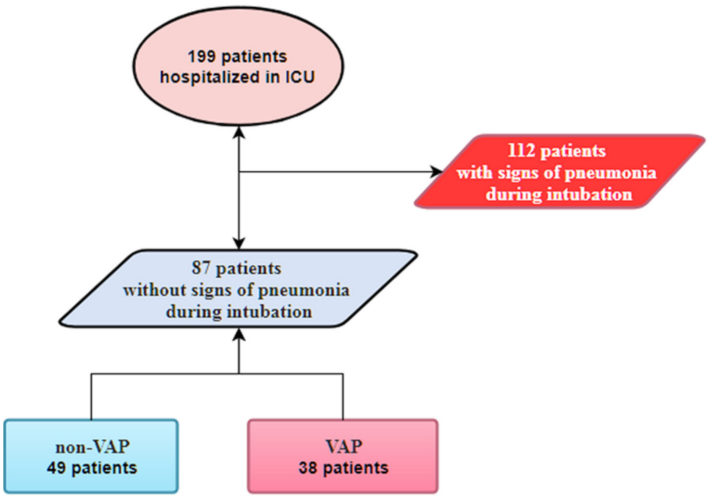

Figure 1. Flowchart

The mortality rate of 49 patients non-VAP was found to be 49% (24/49). Mortality rates were significantly higher in VAP patients ($p<0.05$). Patients who were followed up with a diagnosis of VAP had multiple concurrent diagnoses when they were admitted to the ICU. The distribution of these diagnoses is 27.9% (19) pneumonia, 17.6% (12) neurological diseases, 17.6% (12) respiratory failure, 10.3% (7) congestive heart failure, 8.8% (6) malignancy, 7.4% (5) chronic obstructive pulmonary disease, 5.9% (4) ischemic heart disease, 4.4% (3) septicemia. No significant difference was found between the two groups in terms of comorbidity (diabetes mellitus, chronic obstructive pulmonary disease) status of the patients ($p>0.05$).

When the two patient groups were compared according to the days of hospitalization, the length of ICU stay of patients with VAP was 34.39±5.55 and the days of hospitalization of the group non-VAP were 8.35±5.63. The length of ICU stay time was significantly higher in patients who developed VAP ($p<0.05$).VAP development was observed in patients after intubation at an average of 10.87±7.10 days. Five different types of microorganisms causing VAP were detected in the ICU. Pseudomonas aeruginosa (25%) was the most common of these. The distribution of infectious microorganisms is as shown in Table 2. According to the antibiogram, the susceptibility of these microorganisms to antibiotics is listed in Table 3 and the resistance states are listed in Table 4. Mortality rates of patients compared to isolated microorganisms were compared. All patients isolated from Klebsiella spp. were found to have died.Mortality rates were calculated as 80% for Enterobacter spp, 70.6% for Pseudomonas aeruginosa and 57.1% for Proteus spp. Since Staphylococcus aureus was isolated in only one patient, the mortality rate was not considered.

Table 1. Demographic characteristics of the patients

	non-VAP (n= 49)		VAP (n= 38)		p
Age (year) (mean±SD)	71.22±14.67		72.05±14.184		0.792
Gender (Male/Female)	28/21		22/16		0.559
Primary disease	**n**	**%**	**n**	**%**	
Cardiac diseases	4	8.2	5	13.2	
Malignancy	5	10.2	4	10.5	0.761
Neurological diseases	6	12.2	6	15.8	
Septicemia	1	2.0	2	5.3	
Respiratory diseases	33	67.3	21	55.3	
Mortality (n-%)	**24(49%)**		**29(76.3%)**		**0.008**
APACHE II score (mean±SD)	24.86±8.18		26.13±6.85		0.372
Length of ICU stay (day)	**8.25±5.633**		**34.39±25.55**		**0.000**

VAP: Ventilator-associated pneumonia. ICU: Intensive care unit

Table 2. Distribution of microorganisms isolated from endotracheal aspirate samples in patients developing VAP

Microorganism	n	%
Pseudomonas aeruginosa	17	25
Klebsiella spp.	8	11.8
Proteus spp	7	10.3
Enterobacter spp.	5	7.4
Staphylococcus aureus	1	1.5

Table 3. Sensitivity of VAP agent microorganisms to antibiotics

Antibiotics	General Sensitivity (%)	Microorganisms				
		PAE (%)	Klebsiella spp. (%)	Proteus spp. (%)	Enterobacter spp. (%)	Staphylococcus aureus (%)
Colistin	39.47	23.53	25.00	71.43	60.00	100.00
Cefoxitin	39.47	29.41	12.50	85.71	60.00	-
Imipenem	31.58	41.18	25.00	42.86	-	-
Sefaperazon-Sulbaktam	28.95	11.76	37.50	28.57	40.00	-
Tigecycline	31.58	17.65	25.00	42.86	60.00	-
Ciprofloxacin	26.32	23.53	25.00	28.57	40.00	-
Gentamicin	28.95	23.53	12.50	28.57	60.00	100.00
Amikacin	26.32	29.41	12.50	42.86	20.00	-
Piperacillin-Tazobactam	21.05	17.65	37.50	14.29	20.00	-
Ceftazidim	13.16	5.88	-	42.86	20.00	-

VAP: Ventilator-associated pneumonia, PAE:Pseudomonas aeruginosa

Table 4. Resistance states of VAP agent microorganisms to antibiotics

Antibiotics	General Sensitivity (%)	Microorganisms				
		PAE (%)	Klebsiella spp. (%)	Proteus spp. (%)	Enterobacter spp. (%)	Staphylococcus aureus (%)
Colistin	26.32	41.18	12.50	14.29	20.00	-
Cefoxitin	26.32	29.41	12.50	-	20.00	-
Imipenem	28.95	23.53	25.00	14.29	80.00	-
Sefaperazon-Sulbaktam	10.53	23.53	-	-	20.00	-
Tigecycline	5.26	5.88	-	14.29	-	-
Ciprofloxacin	55.26	70.59	50.00	28.57	60.00	-
Gentamicin	42.11	47.06	37.50	42.86	40.00	-
Amikacin	23.68	17.65	-	14.29	60.00	-
Piperacillin-Tazobactam	36.84	23.53	25.00	28.57	40.00	-
Ceftazidim	42.11	47.06	50.00	28.57	40.00	-

VAP: Ventilator-associated pneumonia, PAE:Pseudomonas aeruginosa

Discussion

Patients monitored at the ICU are prone to infections due to age, underlying diseases, invasive interventions, and sedation [9]. VAP is a common and severe complication and can lead to prolonged length of ICU stay, increased medical costs, and a higher risk of mortality [10]. The use of antibiotics in ICUs can effectively reduce VAP incidence by eliminating pathogenic bacteria, but can also lead to an increase in drug resistance [11].

In our study, the VAP incidence was determined as 43.70%. The reason for this height was evaluated as the majority of the patients followed in our unit were elderly palliative care patients. Because of these patients, the average age of the patients high and length of ICU stay was long in our unit. However, our study results are still compatible with the literature. In a study conducted on 220 patients monitored in the ICU, the VAP rate was reported to be 51.36%. In the same survey, it was stated that the development of VAP increased the duration of the mechanical ventilator, the length of ICU stay, the use of antibiotics and mortality [7]. In another study on 232 patients, the VAP rate was reported as 43.3% [12].

In literature scans, VAP incidence rates varied considerably according to the population included in the study. High VAP rates have been reported in cancer patients [13]. Higher rates of VAP develop in patients with major trauma injury patients, chronic obstructive pulmonary disease patients, Acute Respiratory Distress Syndrome and patients receiving Extracorporeal membrane oxygenation [14].

The long duration of mechanical ventilator is a significant risk factor in VAP development. While the prolongation of ICU stay increases the risk of VAP, every day due to mechanical ventilation increases the risk of VAP by 1-3% [15].

In our study, a significant relationship was found between hospitalization time and VAP development. While the length of ICU stay was 8.25 ± 5.63 days in non-VAP patients; The patients who developed VAP were 34.39 ± 25.55 days. The length of ICU stay was significantly higher in patients who developed VAP.

It has been reported that the risk of developing VAP increases between the 5th and 9th days of mechanical ventilation, and the cumulative incidence is closely related to the total mechanical ventilation time [16]. In the patients included in our study, an average of 10.87 ± 7.10 days after the intubation procedure, infection was observed. Our results are compatible with the literature. We think that long-term ventilation with mechanical ventilator significantly increases the incidence of VAP. To avoid VAP formation, focus should be on preventing intubation and limiting exposure to invasive mechanical ventilation [17].

In a study evaluating 1735 patients who were mechanically ventilated for 48 hours or more, no risk of high VAP was detected in elderly patients by logistic regression analysis [18]. There are also studies in the literature where age is considered a risk factor for VAP development [19, 20]. In our study, no significant difference was found between the mean age of VAP patients and non-VAP patients. The reason for this was evaluated as the majority of patients followed up in our unit were geriatric age group patients.

In a meta-analysis in France, male gender was identified as an independent risk factor for VAP [21]. Many studies have also reported that there is no significant relationship between gender and VAP development [19, 22]. In our study, no significant association was found between gender and VAP development.

In the literature, it has been shown that more VAP develops in patients with a high APACHE II score. In the same study, it was stated that length of ICU stay and mortality rates were higher in these patients [23].

In our study, no significant relationship between the APACHE II score and VAP development was determined because the mean age of the patients in our unit was high.

There are important discussions about the extent to which VAP contributes to death in ICU patients. In many studies conducted in different patient populations in the ICU, no relationship was found between VAP and ICU mortality[13, 16, 24]. In contrast, VAP is directly associated with prolonged mechanical ventilation times and length of ICU stay [14]. In a study evaluating 606 patients, VAP development was found to be associated with high mortality and morbidity rates [19]. In our study, in accordance with the literature, the mortality rate was significantly higher in patients who developed VAP.

In our study, Pseudomonas aeruginosa (25%) was the most isolated microorganism in patients who developed VAP. This result was compatible with the literature. Pseudomonas aeruginosa has been shown to be the most common cause of nosocomial infection and is directly related to increased mortality due to pneumonia in ICUs [25].

Other microorganisms most frequently isolated from tracheal aspirate cultures in our unit are Klebsiella spp. (11.8%) and Proteus spp. (10.3%). When VAP factors are investigated in ICUs, we can face different factors in each unit. In a study conducted in the General ICU, Acinetobacter baumannii (31%), Pseudomonas aeruginosa (20.6%) and Klebsiella spp. (17.2%) were shown as the most frequently isolated VAP factors. [20]. In another study, Klebsiella spp. (22.71%) and Acinetobacter spp. (18.28%) were isolated as the most common VAP agents. [26]. In another study, Acinetobacter baumannii (24.5%), Escherichia coli (14.1%) and Pseudomonas aeruginosa (12.7%) were reported as the most VAP factors.

The relationship between the microorganisms isolated and mortality in our study is compatible with the literature. Pseudomonas pneumonia has been associated with high mortality rates, such as 65% and 87% [15, 25]. In another study, Pseudomonas aeruginosa, Klebsiella spp, Enterobacter spp and Staphylococcus aureus have been associated with high mortality rates [27].

In our study, it was seen that the sensitivity rates of microorganisms isolated to common antibiotics were low and resistance rates were high. These situations and rates were compatible with the literatüre[12, 28]. The reason for this was evaluated as the failure to fully comply with the antibiotic policy set by the infection committee in our unit.

Study limitations

The small size of the sample, the fact that we were not able to obtain microbiological data in some patients although they were ventilated by a mechanical ventilator and there were signs of infection (we think this was due to insufficient tracheal aspirate in these patients) are the limitations of our study.

Conclusion

Today, although many measures and a wide variety of antibiotics have been developed to reduce hospital infections, VAP is still a condition affecting the morbidity and mortality status of patients who are being followed up in ICUs. VAP is associated with mechanical ventilator time, length of ICU stay, and antibiotic use. Strategies to limit exposure to invasive mechanical ventilation and to shorten the duration of intensive care hospitalization should be developed.

Infection control measures should be updated according to the conditions of the unit, strictly adhering to the antibiotic policy in the use of antibiotics to reduce the reported high resistance rates.

Conflict of interests
The authors declare that there is no conflict of interest.

Financial Disclosure
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Ethical approval
Istanbul Yeni Yuzyil University Ethics Committee approved the study.(Date: 12.05.2020 Number: 2020/0405)

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