ACTA FACULTATIS
MEDICAE NAISSENSIS

UDC: 616.24-002:615.816.2.06
DOI: 10.5937/afmnai38-28766

Original article

Evaluation of Pneumonia due to Mechanical Ventilation and its Association with the Severity of Disease in Patients Admitted to Intensive Care Unit

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SUMMARY

Among the hospital-acquired infections, ventilator-associated pneumonia (VAP) has the highest mortality and morbidity rates. The aim of this study was to identify VAP in the intensive care unit (ICU) and its association with the severity of the disease.

This descriptive-analytic study was conducted in Golestan University of Medical Sciences (Northern Iran). In the present study, 239 patients undergoing mechanical ventilation hospitalized in ICU were selected through non-random sampling. Data were recorded by using APACHE II criteria and diagnosis of VAP was made based on clinical criterion and physician confirmation. Data were analyzed by independent t-test, Chi-square test, Mann- Whitney test, and single-variable logistic test.

The incidence of VAP was 19.2% and it was significantly related to mean arterial pressure (P = 0.035) and male sex (P = 0.122). There was a significant and direct correlation between the incidence of VAP and the increase in the value of gastric residual volume > 200 ml (P = 0.001).

The findings of this study showed that male sex, increased arterial pressure, and gastric residual volume were the risk factors for the development of of VAP.

Key words: **pneumonia, ventilator-associated, APACHE, intensive care units, respiration, artificial, incidence**

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INTRODUCTION

Despite many advances in the field of control and prevention, hospital infections stand for a major health problem that remains the most important side-effect of treatment, and they significantly increase mortality, organ dysfunction, and health care costs (1). According to the US Center for Disease Control and Prevention, approximately 1.7 million patients are annually infected with hospital infections, and one in 17 patients treated for the infection dies (2). Hospital-acquired pneumonia is the second most commonly reported infection in the whole department of hospital and the most commonly reported hospital infection in the intensive care unit (ICU). 0.1- 0.5% of the total number of hospitalized patients and 15 - 20% of the patients in the ICUs are affected by the infection (3). The increase of infection in ICU is due to the patient's connection to mechanical ventilation, which raises the risk of pneumonia 10-20 times more compared to patients without attachment to the device (4). Ventilator-associated pneumonia (VAP) is a lung infection that occurs in a patient under mechanical ventilation with tracheotomy or tracheostomy. VAP can develop after more than 48 hours in patients weaning from mechanical ventilation (5). Ventilator-associated pneumonia is the leading cause of death in hospital, and the incidence rate of mortality depends on the immune system. VAP due to *Pseudomonas aeruginosa* resistance to antibiotic and methicillin-resistant *Staphylococcus aureus* (MRSA) was reported in 24-70% of cases. Also, VAP increases mortality rate, the duration of attachment to the mechanical ventilation device, the length of hospital stay in the ICU, re-admission in the hospital, and medical expenses (6). These infections in the United States lead to 1.75 million additional hospital admissions and 1.5 billion dollars additional costs (7). Considering the difference in the implementation of hospital infection control programs and the quality of nursing care in different countries, especially in the developing countries, the incidence of VAP varies. The prevalence of VAP in European countries was reported in 7% of patients undergoing mechanical ventilation. In developing countries, VAP was reported to range from 10% to 41% (8). In a study in India, ninety-five (38%) patients who were ventilated for more than 48 hours developed VAP (9). In Iran, Nassaji et al., in a descriptive analytical study, reported that the incidence of VAP in patients over 15 years of age admitted to the ICU in the university hospitals in Semnan was 9.2%, of which 32.9% were under mechanical ventilation, and 4% of patients without mechanical ventilation suffered pneumonia and the incidence of VAP was 6.7 times higher than in other patients (10). In a study with the aim of determination of the incidence of VAP and bacterial resistance in the ICU in Sanandaj (West of Iran), secretion samples of the endotracheal tube of 149 patients 48 hours after admission revealed 32.2% positive cultures; VAP was confirmed (11). Various modifiable and non-modifiable risk factors are reported for VAP such as age, sex, underlying diseases, accumulation of bacteria in the pharynx and mouth, supine position, taking anti-reflux, anti-acid drugs, pain reliever and antibiotics. Also, repeated tracheal intubation, gastric nasal tube, smoking, drug use, and Glasgow coma score (GCS) have been mentioned as risk factors (12). Retrospective study of risk factors of VAP in 1,872 patients showed that VAP was demonstrated in 23% of all patients treated in ICU, and patients with chronic obstructive pulmonary disease (COPD), obesity, diabetes, and alcoholism were at high-risk (13). Data on outcomes of patients receiving mechanical ventilation in Iran are few, hence the purpose of this study was to determine pneumonitis caused by mechanical ventilation and its relationship with the severity of the disease in hospitalized patients in ICUS.

PATIENTS AND METHODS

This analytic study was conducted in 2018. The population of the study consisted of patients with mechanical ventilation in the ICUs.

Research settings were adult ICU patients in two referral educational hospitals (Golesatn University of Medical Sciences) and one non-teaching hospital (in Golestan province); North of Iran). Considering 95% confidence interval and accuracy (0.05) as well as the estimated 32% for the incidence of VAP, the sample size was 239 patients. The research samples were patients who met inclusion criteria: A) mechanically ventilated patients admitted to the ICU; B) age over 15 years; C) having an artificial airway for more than 48 hours; D) no respiratory infection at the start of the study. Exclusion criteria: A) being less than four days in the study: transfer to another unit, death, weaning from mechanical ventilation; B) pneumonia in the first 48 hours of mechanical ventilation.

Data collection tool: A data registration form was used to collect data: age, sex, clinical status of patients, APACHE scoring (disease severity), frequency of gastric residual volume before each gavage.

Method of collecting data: To conduct the study, after the approval of the research project and ethics committee, the sampling was started. Non-random sampling method was applied.

In this study, the severity of the disease was measured using the APACHE II scale. This scale assesses acute physiological condition and chronic health situation which is used to predict the mortality rate by evaluating the age, physiological condition, and chronic health conditions in the ICU (14). This scoring is based on data related to body temperature, arterial blood pressure, heart rate, respiratory rate, FiO2, PaO2, PCO2, PH, hematocrit (Hct) percentage, white blood cell count (WBC), GCS, blood levels of sodium, potassium, creatinine, and the underlying disease. The amount of stomach residual volume was also routinely recorded before each gavage. Also, in case of pneumonia at the first 24 hours of study or death, discharge or transfer in the first four days of the study, a patient was excluded. Patients were monitored for gastric residual or clinical symptoms of pneumonia during the entire duration of hospitalization. After confirmation by physician, the presence of gastric residual and pneumonia symptoms were recorded as cases of pneumonia.

Data analysis method: Data was collected and analyzed by SPSS software version 16. The incidence of pneumonia was reported in terms of 95% confidence interval. The relationship between incidence and qualitative variables was evaluated by Chi-square test and the relationship between incidence and quantitative or numerical variables was measured (in the case of normalization) by independent T-test or (in the absence of normalization) by Mann Whitney test. Logistic regression and odds ratio (OR) were used to examine the simultaneous effects of variables on the incidence of pneumonia. In all tests, a significance level of 0.05 was considered.

Ethical consideration

All principles of accepted Code of Ethics such as informed consent form were considered. The ethics committee approval code was IR.GOUMS.REC. 1395.291.

RESULTS

A total of 255 patients were enrolled in the study, 15 of whom lost the criterion of continuing the study due to less than 96 hours of hospitalization, and as a result, replacement was performed. One patient was considered as a highly deviant data due to hospitalization for 6 months and did not enter the data analysis. Out of 239 patients, 160 (66.9%) were male, mean age was 58.53 ± 20.76 years, mean hospital stay was 19.75 ± 21.35 days, mean GCS of patients was 6.53 ± 6.33 and mean APACHE score was 39.3 (22.07 ± 7.39). The incidence of VAP was 19.2%. Of the patients studied, 67.9% died and other patients were transferred to another units or were discharged.

Table 1 describes the physiological variables. The variables were normalized using Shapiro-Wilk and Kolmogorov-Smirnov tests. The results indicated that the mean arterial pressure and Hct were in normal distribution in both groups of patients with and without VAP. The mean and standard deviations (SD) of arterial pressure in the VAP group were 98.58 ± 18.77 and 91.73 ± 19.9, respectively, which according to the independent t-test these was significant (p-value = 0.035). As for other variables, the results did not show a significant difference between the two groups.

In the study of the relationship between age and pneumonia caused by mechanical ventilation, first the age variable was described in different groups, then due to the abnormality of the age variable, the Mann-Whitney test was used. The results showed that the mean age variable was not significant in both groups (p value = 0.91).

The findings of Table 2 show that according to the Chi-square test, there is no significant relationship between VAP and the cause of mechanical ventilation (decreased consciousness, decreased SPO2, after the operating room, after cardiopulmonary resuscitation) (p-value = 0.51).

The mean and standard deviation of APACHE score was 22.07 ± 7.39. Data analysis using Chi-square test showed that there was no significant relationship between VAP and disease severity in the patients (p value = 0.72).

A single-variable logistic analysis test was used to determine the relative frequency of pneu-

Table 1. *Relationship between VAP and physiological variables*

Physiological variables	P-value	statistical test	VAP	
			No (N = 193)	Yes (N = 47)
			Mean ± SD	Mean ± SD
Temperature	0.5	*Mann–Whitney* U *test*	37.30 ±0.52	37.34± 0.083
Average arterial pressure	0.035	*Student's t-test*	91.73 ±19.9	98.58± 18.77
Heart beat	0.63	Mann–Whitney *U* test	95.50 ±21.28	98.32± 25.46
Number of breaths	0.36	Mann–Whitney *U* test	18.86 ±6.61	19.67± 6.49
Arterial Oxygen Pressure	0.23	Mann–Whitney *U* test	81.81 ±62.98	69.57± 55.3
PH	0.14	Mann–Whitney *U* test	7.30 ±0.45	7.33± 0.11
Potassium (K)	0.17	Mann–Whitney *U* test	4.10± 0.68	0.95± 4.11
Sodium (Na)	0.85	Mann–Whitney *U* test	139.76± 6.34	140.08± 5.93
Hematocrit (Hct)	0.4	Student's t-test	34.45± 6.22	33.58± 6.8
WBC	0.12	Mann–Whitney *U* test	13.91± 7.33	15.10± 6.64
GCS	0.31	Mann–Whitney *U* test	6.64± 3.04	6.23± 3.14
Creatinine (Cr)	0.34	Mann–Whitney *U* test	1.63± 0.1	1.83± 0.23

Table 2. *The relationship between VAP and the cause of mechanical ventilation and disease severity*

The cause of mechanical ventilation	Pneumonia		Test
	No	Yes	
	Frequency (%)	Frequency (%)	$\chi^2 = 2.31$ Df = 3 P-value = 0.51
Reduced alertness	103 (79.2)	27 (20.8)	
Reduce SPO2	46 (78)	13 (22)	
After the operating room	11 (91.7)	1 (8.3)	
After CPR	33 (86.8)	5 (13.2)	
Severity of disease			
Mild (15 - 0)	37 (19.2)	8 (17.4)	$\chi^2 = 1.31$ Df = 3 P-value = 0.72
Medium (19 - 16)	34 (17.6)	6 (13)	
Intense (30 - 20)	102 (52.8)	25 (54.3)	
30 Very intense >	20 (10.4)	7 (15.2)	

Table 3: *Determination of the risk of VAP*

	VAP		Test	OR	CI 95 % OR
Sex	No	Yes	$\chi^2 = 6.31$ Df = 1 P-value = 0.012	2.76	1.22 - 6.25
	Frequency (%)	Frequency (%)			
Female	71 (36.8)	8 (17.4)			
Male	122 (63.2)	38 (82.6)			

Table 4. *Determination of the probability of increased pneumonia due to VAP with increased arterial pressure*

Medium arterial pressure	VAP		Test	OR	OR (CI 95%)
	No	Yes	P-value = 0.037	1.02	1.001 – 1.034

monia in terms of gender in hospitalized patients in the ICUs (Table 3).

The findings showed that the risk of VAP in males was 2.76 times higher than in females.

A single-variable logistic analysis was used to determine the probability of increased VAP with increasing arterial pressure in patients admitted to the ICUs. Table 4 shows that the probability of an increase in VAP with increase in arterial pressure unit is 1.02 times higher.

In this study, the incidence of relative frequency of late-onset (4 days and more) and early-onset pneumonia (less than 4 days) was 15.9% and 3.3%, respectively.

Data analysis using Mann-Whitney test showed that there was a significant correlation between VAP and lavage frequency due to gastric residual volume (p value ≤ 0.001).

DISCUSSION

In this study involving 239 patients admitted to ICUs, VAP was reported in 19.2% of them; 3.3% was assigned to early-onset pneumonia and 15.9% to late-onset pneumonia. Reported cases vary between 5% and 40% depending on settings and diagnostic criteria. VAP is associated with long-term mechanical ventilation and stay in the ICU (15). However, there is evidence that report the incidence of VAP even with higher percentage. The study by Hedrik et al. in ICUs of a university hospital showed that VAP occurred in 71% of patients with trauma and 29% of patients without that. There was also a significant difference between the clinical outcomes of patients with early-onset pneumonia (less than 96 hours) and late-onset pneumonia (more than 96 hours) and patients with trauma (16). In the current study, there was no significant correlation between APACHE II score among patients with VAP and without that. In the study of Chao et al., there was no significant relationship between APACHE II score and VAP (17), while this relationship was significant in Ranjbar et al.'s study (18). In a 12-year retrospective cohort study by Liang et al. in China, APACHE-II score, successful weaning, and nosocomial infection in the ICU were independently associated with the prognosis of patients given mechanical ventilation in the ICU (19). Although the age of 60 and above is expected to be one of the factors influencing the incidence of VAP, in the present study, there was no significant relationship between them. In the study of Nobahar et al. and Chao et al., there was no meaningful relationship between the demographic variables of age with VAP (20, 17). In a prospective observational, a case-control study by Othman et al. on forty-eight adult patients, VAP was developed in 35.4%, but there was no statistically significant difference between VAP and non-VAP groups regarding the age and sex (21). Concerning a significant relationship between sex and VAP, pieces of evidence are not unanimous. In some cases, male sex was reported as a risk factor for developing pneumonia (22), while in study by Nobahar et al. (20), gender had no effect on the incidence of VAP (p = 0.63). In our study, the relationship between the male sex with VAP was significant and the results showed that male sex increased the chance of pneumonia by 2.76 times.

Review paper by Wu et al. on the international risk factors of VAP showed that the patient characteristics, mechanical ventilation time, length of hospital stay, GCS, and other comorbidities were not only the independent risk factors of VAP but also had influence on each other (23). Clinical outcomes observed in ICUs from two university hospitals in Ankara (Turkey) in patients with mechanical ventilation receiving intestinal nutrition suggested that gastric residual volume (GRV) measurement is not a reliable measure for tolerating nutrition and reflux and it is not necessary to use it as part of care standard in specialized care units (24). The effect of GRV on the frequency of VAP in 150 adult patients admitted to the ICU showed that increased GRV did not result in increased rates of VAP (25). However,

in the present study, the qualitative criterion of having or not having the remaining amount of lavage in the routine for patients prior to each gavage is used and there was a significant relationship between VAP and the presence of GRV. In Liu et al.'s study, APACHE II score was one of risk factors of VAP infection for patients who received mechanical ventilation ($P < 0.05$) (26).

Research limitation: In the present research, teaching and governmental ICUs were studied but not the private ones; hence, the results may not be generalized to all settings. After discharging patients from ICU and transferring to the general ward, monitoring stopped, therefore, there was a possibility of late-onset pneumonia.

CONCLUSION

The findings of this study regarding the determination of the incidence of VAP in patients admitted to the ICU showed that the incidence of VAP is not related to disease severity (APACHE score), while moderate arterial pressure and gender (male) has been related. Also, the incidence of VAP was significantly associated with the number of lavages (GRV).

Acknowledgment

This article was derived from a master thesis and the research project was approved at the deputy of research and technology of Golestan University of Medical Sciences. The authors sincerely thank the patients who participated in this study.

Financial support and sponsorship

Golestan University of Medical Sciences (478 - 6).

Conflicts of interest

There is no conflict of interest.

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Procena pneumonije usled mehaničke ventilacije i njena veza sa težinom bolesti kod bolesnika primljenih na jedinicu intenzivne nege

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SAŽETAK

Među bolničko stečenim infekcijama, pneumonija povezana sa mehaničkom ventilacijom (eng. – VAP) beleži najviše stope mortaliteta i morbiditeta. Cilj ove studije bilo je otkrivanje pneumonije povezane sa mehaničkom ventilacijom na jedinici intenzivne nege (eng. – ICU) i njene povezanosti sa težinom bolesti.

Deskriptivno-analitička studija urađena je na Univerzitetu medicinski nauka u Golestanu (severni Iran). Za potrebe ove studije metodom neslučajnog uzorkovanja izabrano je 239 bolesnika na mehičkoj ventilaciji koji su hospitalizovani na jedinici intenzivne nege.

Podaci su prikupljeni prema APACHE II kriterijumima, a dijagnoza VAP-a je uspostavljena na osnovu kliničkog kriterijuma, a potvrđena fizičkim pregledom. Podaci su anlizirani upotrebom t-testa, Chi-square testa, Mann- Whitney testa, i logističkim testom pojedinačne varijable.

Incidencija VAP-a iznosila je 19.2% i bila je značajno povezena sa srednjim arterijski pritiskom (P = 0.035) i muškim polom (P = 0.122). Utvrđena je signifikantna i direktna korelacija između incidencije VAP-a i povećanja rezidualnog gastričnog volumena > 200 ml (P = 0.001).

Nalazi ove studije pokazali su da su muški pol, povišen arterijski pritisak i rezidualni gastrični volumen bili faktori rizika za razvoj VAP-a.

Ključne reči: **pneumonija, povezana sa ventilacijom, APACHE, jedinice intenzivne nege, respiracija, veštački, incidencija**