Journal of Pharmaceutical Care
jpc.tums.ac.ir

A Comparative Study of the Prevalence of Bacterial Strains in Early and Late-Onset Ventilator-Associated Pneumonia in Critically Ill Patients

Babak Alikiaie[1], Daryoush Moradi[1], Sarah Mousavi[2], Seyed Taghi Hashemi[1*], Maryam Mosaddeq[3]

[1] Department of Anesthesiology and Intensive Care, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
[2] Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.
[3] Student of Medicine, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
Received: 2016-10-12, Revised: 2016-11-26, Accept: 2016-11-28, Published: 2016-12-01

ARTICLE INFO

Article type:
Original article

Keywords:
Ventilator-Associated Pneumonia
Prevalence
Acinetobacter Baumannii

ABSTRACT

Background: This study aims to determine the prevalence of early (less than 4 days of hospitalization) –and late-onset (more than 4 days after hospitalization) ventilator-associated pneumonia in the intensive care units of Al-Zahra center in Isfahan.
Methods: Through a prospective study, 100 patients with ventilator-associated pneumonia who were hospitalized in the intensive care units of Al-Zahra hospital during 2015 were investigated, and early and late onset pneumonia were determined. Moreover, the etiology of bacterial strains and other clinical and demographic characteristics were compared in two groups.
Results: The patients, 23 and 77 suffered from late –and early-onset pneumonia, respectively. The mean score of pneumonia in the two groups (early –and late-onset pneumonia) was 7.3± 2.1 and 7.2±1.6, respectively, which showed no significant difference (P: 0.8). The most common types of bacteria that caused pneumonia were methicillin-resistant *Staphylococcus aureus* (MRSA) (43% of frequency) and *Acinetobacter Baumannii* (34% of frequency) in early –and late-onset pneumonia, respectively. However, the frequency distribution of the type of bacteria by the type of pneumonia was not significantly different (P:0.1).
Conclusion: A significant percentage of pneumonia in intensive care units are of early-onset type, which can lead to patients' prolonged hospitalization in intensive care units and it may be lead to increased mortality rate among them. Therefore, it is recommended that the patients hospitalized in intensive care units should be carefully examined in terms of the occurrence of pneumonia symptoms.

J Pharm Care 2016; 4(3-4): 64-69.

► Please cite this paper as:
Alikiaie B, Moradi D, Mousavi S, Hashemi ST, Mosaddeq M. A Comparative Study of the Prevalence of Bacterial Strains in Early -and Late-Onset Ventilator-Associated Pneumonia in Critically Ill Patients. J Pharm Care 2016; 4(3-4): 64-69.

Introduction

Pneumonia is the second most common cause of acute hospital infection that accounts for about 15% of all acute hospital infections in the world. Pneumonia is the most common infection in intensive care units (ICU) with a prevalence rate of 1-20% (1).According to the World Health Organization, pneumonia is the most common cause of infection in ICUs (2). Over 90% of ICU-acquired pneumonia belongs to mechanically ventilated patients

* *Corresponding Author*: Dr Seyed Taghi Hashemi
Address: Department of Anesthesiology and Intensive Care, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Hezar Jerib Avenue, Isfahan, Iran. Tel:+983117922532.
E-mail: st_hashemi@med.mui.ac.ir

(3), so pneumonia is observed 6-21 times more in such patients (4). According to a study, 86% of ICU-acquired pneumonia is related to mechanical ventilation and 250-300'000 people in the United States are suffering from it, and it is observed in 5-10 cases per 1000 patients admitted to hospitals (5,6).The patients hospitalized in ICUs are at risk of death, both because of underlying diseases and secondary factors such as pneumonia (7).Ventilator-associated pneumonia (VAP) is a type of hospital pneumonia, which is, specifically speaking, a lung infection that occurs in intubated patients or ventilated patients with tracheostomy 48 hours after hospitalization (8).

In 2002, the organization for hospital acquired infections reported the rate of VAP to be 2.2%. Moreover, the Centers for Disease Control and Prevention (CDC) reported the rate of VAP to be 3.6 per 1000 patients (9-10). In undeveloped countries, this rate is reported to be 7.41-10 per 1000 ventilator days (11). On the other hand, VAP is the most important cause of morbidity, increased mortality, hospital cost, and length of stay (12).

Various studies report the mortality rate of VAP to be 0-50% (13-15). However, another study reports the mortality rate of VAP to be about 24-50% (16). Moreover, VAP increases the length of stay in ICUs by about 9 days (17). Prolonged hospitalization and treatment cause hospital cost. According to a study, the estimated hospital cost for each person is $11.879 (18). According to another study, the estimated cost is about $40'000 (19).

VAP is divided into two types, namely early –and late-onset. The early –and late-onset VAP are observed less than 4 days and 4 days after hospitalization, respectively (20). The early-onset VAP has better prognosis and its strains show a better response to treatment. However, it seems that the prevalence and mortality rate of the late-onset VAP is higher and its drug resistance has increased among patients (21).

Although provision of solutions in recent years has decreased the prevalence of VAP, it is still an ongoing issue (22-23). Therefore, this study aims to determine the prevalence of early –and late-onset ventilator-associated pneumonia in the intensive care units of Al-Zahra center in Isfahan.

Methods

This study was a cross sectional study which was conducted at Al-Zahra hospital in Isfahan during January to December of 2015. The study population consisted of ventilated patients hospitalized in the ICUs of this center.

The inclusion criteria were as follows: no underlying lung disease, at least 18 years of age, hospitalized in ICU, and possibility of sampling, lack of facial fractures, no HIV (human immunodeficiency) infection, and obtaining consent from the patient's relatives to participate in the study. Moreover, the patient was decided to be excluded from the study if he/she died before sampling or if his/her relatives declared that he/she did not consent to participate in the study.

The required sample size was estimated to be 100 individuals by using the sample size formula for prevalence study and by considering confidence interval = 95%, the prevalence of Gram-negative bacteria in ventilator-associated pneumonia = 0.5, and acceptance of 0.1 errors.

After approving the draft plan and obtaining permission from the Research Council and Ethics Committee of the Isfahan University of Medical Sciences, the patients' relatives were provided with the necessary oral explanations about the study, and then informed consent forms were obtained from them.

All nursing care, anesthesia services, oral health care, and ventilator connections were done accurately and as usual. First, patients' demographic characteristics such as age, gender, and cause of hospitalization in ICU were determined and then recorded in the data collection form.

The patients who had symptoms of lung infection during the first 48-96 hours and after 96 hours were examined, and diagnosis of VAP was based on the CDC (the Centers for Disease Control and Prevention) guideline (20). According to these criteria, to diagnose VAP, at least one of the following criteria must be observed in patients: 1) Fever above 38°C with no other reason. 2) White blood cell count ranging from 4000 to 12000. 3) Altered mental status in people over 70 years of age with no other reason. 4) Progressive changes 48 hours after using the ventilator for at least two consecutive chest x-rays. 5) Observation of at least two criteria out of the following four criteria (1: purulent sputum or changes in respiratory secretions. 2: Exacerbation of cough, shortness of breath, and tachypnea. 3: crackling sound. 4: deterioration of the patient's respiratory status) (21). Moreover, the samples obtained from the patients were sent to the hospital's laboratory and then were cultured in blood and MacConkey agar culture media.

The samples were cultured in qualitative culture media within the timeframe of respiratory infections culture. After 48 hours, these media were examined in terms of the growth of microorganisms. The plates were assessed by a clinical microbiologist expert at culturing respiratory samples. Also the degree of alertness was evaluated by Glasgow coma scale.

Data were collected, entered into the computer, and finally analyzed using SPSS software (version 22, SPSS Inc, Chicago, IL). Quantitative data between the two groups (early- and late-onset pneumonia) were compared using the independent t-test. Pearson's chi-squared test (X^2) was used to compare the frequency distribution of the pathogens causing pneumonia between the two groups. P value lower than 0.05 ($P<0.05$) was considered as the level of significance.

Table 1. Distribution of demographic variables of the type of pneumonia.

Type of pneumonia variable		Late-onset	Early-onset	P Value
Average of age		34.1±11.2	33.77±13.9	0.9
Gender Number (percent)	Male	17 (73.9)	37 (48.1)	0.03
	Female	6 (26.1)	40 (51.9)	
Reason for hospitalization in ICU Number (percent)	Trauma	14(60.9)	39(50.6)	0.4
	Non-traumatic	9 (39.1)	38(49.4)	

ICU: Intensive Care Unit.

Results

In this study, 100 patients diagnosed with VAP were investigated. The patients' mean age was 33.8 ± 13.3. The minimum and maximum age of the patients was 18 and 75, respectively. The mean age of the patients with early and late – onset was 30.8 ± 12.7 and 38.1 ± 13.1, respectively, and no statistical difference between the two groups (P: 0.006).

According to the existing criteria, 23 (23%) and 77 (77%) patients suffered from late-onset and early-onset pneumonia, respectively. The mean pneumonia score in late- and early-onset pneumonia was 7.3 ± 2.1 and 7.2 ± 1.7, respectively. According to the t-test, no significant difference was observed between the two groups (P: 0.8).

Table 1 shows the distribution of demographic variables of the type of pneumonia. According to the results, the mean age of the patients in the two groups (early- and late-onset pneumonia) was not significantly different (P: 0.9); however, sex distribution was different between the two groups. In other words, late-onset and early-onset pneumonia was more prevalent in males and females, respectively. According to Pearson's chi-squared test (X^2), sex distribution of the type of pneumonia had a significant difference (P: 0.03). However, a type of pneumonia by the reason for hospitalization in the ICU did not have a significant difference (P: 0.4).

The Glasgow coma scale (GCS) score of the late- and early-onset pneumonia groups was 7.3 ± 1.7 and 5.9 ± 1.8, respectively. According to the t-test, the level of GCS was significantly higher in patients with late-onset pneumonia (P: 0.001).

The mean acute physiology and chronic health evaluation (APACHE) score in late- and early-onset patients were 16.8±3.14 and 15.8±3.9, respectively. According to the t-test, no significant difference was observed between the two groups (P:0.3) (Table 2). The mean duration of mechanical ventilation in the late- and early-onset pneumonia groups was 11 ± 3.8 and 16.1 ± 5.3 days, respectively. According to the t-test, a significant difference was observed between the two groups (P < 0.001). The mean length of stay in ICU in the two groups was 16.0 ± 5.1 and 21.8 ± 6.1, respectively. According to the t-test, a significant difference was observed between the two groups (P < 0.001) (Table 1).

According to the results, the most common types of bacteria that caused pneumonia were *Acinetobacter baumannii* (33.8% of frequency) and methicillin-resistant *Staphylococcus aureus* (MRSA) (30.4% of frequency) in early –and late-onset pneumonia, respectively. However, according to Fisher's exact test, the frequency distribution of the type of bacteria by the type of pneumonia was not significantly different (P: 0.1).

It is noteworthy that in 13 cases of late-onset pneumonia and 19 cases of early-onset pneumonia, Gram-positive bacteria were the cause of pneumonia (56.5% vs. 24.7%). According to Fisher's exact test, a significant difference

Table 2. Pneumonia variables in early and late onset VAP.

Type of pneumonia variable	Late-onset	Early-onset	P Value
GCS	7.3±1.75	5.9±1.8	0.001
APACHE II score	16.8±3.14	15.83±3.98	0.3
Duration of mechanical ventilation (Day)	16.1±5.3	11±3.8	<0.001
Length of ICU stay (Day)	21.8±6.1	15±5.1	<0.001

APACHE: acute physiology and chronic health evaluation, GCS: Glasgow coma scale, ICU: Intensive Care Unit, VAP: ventilator-associated pneumonia.

Table 3. The frequency of the type of bacteria, Gram staining, and multidrug resistance by the type of pneumonia.

Type of pneumonia variable		Late-onset	Early-onset	P Value
Type of bacteria	MRSA*	7 (30.4)	13 (16.9)	0.2
	Acinetobacter baumannii	6 (26.1)	27 (35.1)	
	Klebsiella pneumoniae	2 (8.7)	7 (9.1)	
	Pseudomonas aeruginosa	2 (8.7)	14 (18.2)	
	Streptococcus pneumoniae	6 (26.1)	7 (9.1)	
	Haemophilus influenzae	0 (0)	4 (5.2)	
	E. coli	0 (0)	5 (6.5)	
Gram staining	Positive	13 (56.6)	19 (24.7)	0.004
	Negative	10 (43.5)	58 (75.3)	
Multidrug resistance	No	17 (73.9)	61 (79.2)	0.6
	Yes	6 (26.1)	16 (20.8)	
Mortality	No	18 (78.3)	74 (96.1)	0.02
	Yes	5 (21.7)	3 (3.9)	

* Methicillin-resistant Staphylococcus aureus.

was observed between the two groups (P < 0.004). On the other hand, in 6 cases of late-onset and 16 cases of early-onset pneumonia, the bacteria causing pneumonia were multidrug-resistant (26.1% vs. 20.8%). However, according to Pearson's chi-squared test (X^2), multidrug resistance by the type of pneumonia was not significantly different (P: 0.6). The results are shown in Table 3.

As the results show, of 100 patients with pneumonia, 8 patients died, among whom 5 and 3 cases suffered from late- and early-onset pneumonia, respectively (21.7% vs. 3.9%). According to Fisher's exact test, the frequency distribution of mortality by the type of pneumonia was significantly different (P: 0.02).

Table 4 shows the frequency distribution of the antibiotic resistance of the strains grown in culture media. Performing Fisher's exact test of these data showed that the resistance of the strains against the studied antibiotics was significantly different except for clindamycin. Moreover, the results of this study showed that among the common Gram-positive bacteria, MRSA infections were sensitive to most antibiotics so that the aforementioned strains were completely sensitive to ciprofloxacin, vancomycin, gentamicin, rifampin, and cefoxitin.

Discussion

The overall goal of this study was to compare the prevalence of bacterial strains in two groups of patients with early- and late-onset ventilator-associated pneumonia and two groups of emergency and non-emergency patients at Al-Zahra hospital in Isfahan. Of the patients, 23 (23%) and 77 (77%) suffered from late –and early-onset pneumonia, respectively. Investigating the clinical and demographic characteristics of the patients by the type of pneumonia showed that patients' age had no significant effect on the type of pneumonia, and the prevalence of the type of pneumonia by sex was significantly different so that late-onset pneumonia was more common in males than in females.

In a study, Aly et al., showed that VAP is the most common hospital-acquired infection in ICUs. Gram-negative bacteria are the most common reported etiologic organisms for infection in ICUs (24). Investigating the epidemiology, etiology, and diagnosis of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) in Asian countries, Chawla et al., concluded that, like in the rest of the world, these two diseases are among the major health problems in these countries. They also concluded that the mortality rate of these two diseases might be so high, and the outcome of patients depends on various factors, especially patients' age and the interval between hospitalization in ICU and pneumonia (25).

Another study reported the incidence of health-acquired pneumonia to be over 50%, which was often observed in elderly patients and those with underlying diseases (25). Examining the clinical characteristics showed that the patients with late-onset pneumonia enjoyed a higher level of consciousness. However, duration of mechanical ventilation and length of stay in ICU was greater in the

Table 4. The Frequency of the antibiotic resistance of the strains grown in culture media.

Antibiotic	Antibiotic resistance	MRSA	Acinetobacter	Klebsiella	Pseudomonas	Streptococcus pneumoniae	Haemophilus influenzae	E. coli	P
Clindamycin	Sensitive	15(75)	0(0)	4944.4)	7(43.8)	11(84.6)	4(100)	0(0)	0.23
	Intermediate	5(25)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
	Resistance	0(0)	0(0)	1(11.1)	7(43.8)	2(15.4)	0(0)	0(0)	
Ciprofloxacin	Sensitive	2(100)	0(0)	0(0)	80(50)	13(100)	4(100)	0(0)	<0.001
	Intermediate	0(0)	0(0)	2(22.2)	1(6.3)	0(0)	0(0)	0(0)	
	Resistance	0(0)	0(0)	3(33.3)	5(31.3)	0(0)	0(0)	0(0)	
Vancomycin	sensitive	2(100)	0(0)	4(44.4)	11(68.8)	11(84.6)	3(75)	0(0)	<0.001
	Intermediate	0(0)	0(0)	1(1.1)	3(18.8)	2(15.4)	1(25)	0(0)	
	Resistance	0(0)	33(100)	2(12.5)	0(0)	0(0)	0(0)	5(100)	
Gentamycin	Sensitive	2(100)	0(0)	4(44.4)	11(68.8)	13(100)	4(100)	0(0)	<0.001
	Intermediate	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
	Resistance	(0)0	0(0)	1(11.1)	3(18.8)	0(0)	0(0)	0(0)	
Co-trimoxazole	Sensitive	19(95)	0(0)	0(0)	4(25)	11(84.6)	3(75)	0(0)	<0.001
	Intermediate	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
	Resistance	1(5)	0(0)	5(55.6)	10(62.5)	2(15.4)	1(25)	0(0)	
Rifampin	Sensitive	2(100)	0(0)	4(44.4)	11(68.8)	13(100)	4(100)	0(0)	<0.001
	Intermediate	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
	Resistance	0(0)	0(0)	1(11.1)	3(18.8)	0(0)	0(0)	0(0)	
Cefoxitin	Sensitive	0(0)	0(0)	1(11.1)	7(43.8)	9(69.2)	3(75)	0(0)	<0.001
	Intermediate	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
	Resistance	2(100)	0(0)	4(44.4)	7(43.8)	4 (30.8)	1(25)	0(0)	
Tetracycline	Sensitive	1(5)	0(0)	0(0)	8(50)	11(84.6)	3(75)	0(0)	<0.001
	Intermediate	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
	Resistance	19(95)	0(0)	5(55.6)	6(37.5)	2(15.4)	1925)	0(0)	
Cefazolin	Sensitive	5(25)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	<0.001
	Intermediate	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
	Resistance	15(75)	0(0)	1(11.1)	3(18.8)	0(0)	0(0)	0(0)	
Ceftazidime	Sensitive	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	<0.001
	Intermediate	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
	Resistance	2(100)	0(0)	1(1.1)	3(18.8)	0(0)	0(0)	0(0)	

MRSA: Methicillin-resistant Staphylococcus aureus.

patients with late-onset pneumonia than in those with early-onset pneumonia.

According to the results of this study, multidrug resistance by the type of pneumonia was not significantly different. However, performing antibiogram test on the strains grown in culture media showed that drug resistance was more dependent on the type of bacteria than the type of pneumonia. On the other hand, as the results of this study show, the mortality rate was significantly higher in the patients with late-onset pneumonia.

In their study Ibrahim et al., concluded that both early- and late-onset VAP increase mortality rate and length of hospitalization. Moreover, both groups had similar pathogens, and *Pseudomonas aeruginosa* and drug-resistant *staphylococcus aureus* were among the important pathogens of early-onset pneumonia (26). Hedrick et al., studied a number of trauma patients and patients undergoing surgery who had been hospitalized from 1999 to 2005 and had suffered from pneumonia. They found no difference between the early- and late-onset pneumonia in terms of mortality rate and length of hospitalization. In this study, for non-trauma patients, the mortality rate of late- and early-onset pneumonia was 44% and 23%, respectively. However, for trauma patients, the mortality

rate of late- and early-onset pneumonia was 11% and 41%, respectively, and the length of stay was shorter in trauma patients than in those undergoing surgery (5).

Giard et al., investigated the risk factors affecting the incidence of VAP in 11 ICUs. In their study, the incidence rate of VAP was 13.1% and both types of pneumonia (early- and late-onset) had different risk factors. The risk factors for early- and late-onset pneumonia were diagnostic category and old age and infection before the incidence of VAP, respectively (27).

Examining the characteristics of the bacteria causing pneumonia showed that the most common cause of early- and late-onset pneumonia was Acinetobacter and MRSA, respectively. However, the difference between the two groups was not significant. Moreover, the results showed that Gram-positive and Gram-negative bacteria were the causes of pneumonia in late- and early-onset pneumonia, respectively.

In conclusion, according to the obtained results, it can be concluded that a significant percentage of pneumonia in ICUs is of late-onset type, and this type of pneumonia depends on the factors such as patient's sex, state of consciousness, Gram-negative factors causing pneumonia, and duration of mechanical ventilation. These factors can lead to patients' prolonged hospitalization in intensive care units and increased mortality rate among them. Moreover, although antibiotic resistance pattern was not dependent on the type of pneumonia, antibiotic-resistant strains were more observed among the patients with late-onset pneumonia. Therefore, further studies should be carried out. It is also recommended that all patients hospitalized in ICUs, including trauma and other patients, should be carefully and daily examined in terms of the occurrence of pneumonia symptoms so that they could be treated upon seeing the symptoms.

Acknowledgements

The paper was approved and supported by the Vice Chancellor for Research and Technology, School of Medicine. Hereby the authors of this paper would like to express their sincere gratitude for their unwavering support.

References

1. Bassi GL, Ferrer M, Marti JD, Comaru T, Torres A. Ventilator-associated pneumonia. Semin Respir Crit Care Med 2014;35(4):469-81.
2. Kalanuria AA, Ziai W, Mirski M. Ventilator-associated pneumonia in the ICU. Crit Care. 2014;18(2):208.
3. Restrepo MI, Peterson J, Fernandez JF, Qin Z, Fisher AC, Nicholson SC. Comparison of the bacterial etiology of early-onset and late-onset ventilator-associated pneumonia in subjects enrolled in 2 large clinical studies. Respir Care 2013; 58(7): 1220-5.
4. Enne VI, Personne Y, Grgic L, Gant V, Zumla A. Aetiology of hospital-acquired pneumonia and trends in antimicrobial resistance. Curr Opin Pulm Med 2014;20(3):252-8.
5. Hedrick TL, Smith RL, McElearney ST, et al. Differences in early- and late-onset ventilator-associated pneumonia between surgical and trauma patients in a combined surgical or trauma intensive care unit. J Trauma 2008; 64(3): 714-20.
6. MacVane SH. Antimicrobial Resistance in the Intensive Care Unit: A Focus on Gram-Negative Bacterial Infections. J Intensive Care Med 2017;32(1):25-37.
7. Gillespie R. Prevention and management of ventilator-associated pneumonia – the Care Bundle approach. SAJCC 2009; 25(2): 44-51.
8. Dudeck MA, Weiner LM, Allen-Bridson K, et al. National Healthcare Safety Network (NHSN) report, data summary for 2012, Device-associated module. Am J Infect Control 2013;41(12):1148-66.
9. Timsit JF, Esaied W, Neuville M, Bouadma L, Mourvllier B. Update on Ventilator-associated pneumonia. F1000Res 2017;6:2061.
10. Arabi Y, Al-Shirawi N, Memish Z, Anzueto A. Ventilator-associated pneumonia in adults in developing countries: a systematic review. Int J Infect Dis 2008; 12(5):505-12.
11. Nair GB, Niederman MS. Ventilator-associated pneumonia: present understanding and ongoing debates. Intensive Care Med 2015;41(1):34-48.
12. Mangram AJ, Sohn J, Zhou N, et al. Trauma-associated pneumonia: time to redefine ventilator-associated pneumonia in traumapatients. Am J Surg 2015;210(6):1056-61; discussion 1061-2.
13. Guzmán-Herrador B, Díaz Molina C, Allam MF, Fernández-Crehuet Navajas R. Underlying illness severity and outcome of nosocomial pneumonia: prospective cohort study in intensive care unit. J Hosp Infect 2014;86(1):53-6.
14. Wałaszek M, Kosiarska A, Gniadek A, et al. The risk factors for hospital-acquired pneumonia in the Intensive Care Unit. Przegl Epidemiol 2016;70(1):15-20, 107-10. English, Polish.
15. Oliveira J, Zagalo C, Cavaco-Silva P. Prevention of ventilator-associated pneumonia. Rev Port Pneumol 2014;20(3):152-61.
16. Allen-Bridson K, Gross C, Anttila A, et al. Health care-associated infections studies project: An American Journal of Infection Control and National Healthcare Safety Network data quality collaboration. Am J Infect Control 2017;45(12):1394-1395.
17. Bird D, Zambuto A, O'Donnell C, et al. Adherence to ventilator-associated pneumonia bundle and incidence of ventilator associated pneumonia in the surgical intensive care unit. Arch Surg 2010; 145(5): 465-70.
18. Grap MJ, Munro CL, Unoki T, Hamilton VA, Ward KR. Ventilator-associated pneumonia: the potential critical role of emergency medicine in prevention. J Emerg Med 2012; 42(3): 353-62.
19. Aykac K, Ozsurekci Y, Tanir Basaranoglu S. Future Directions and Molecular Basis of Ventilator Associated Pneumonia. Can Respir J 2017;2017:2614602.
20. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63(5):e61-e111.
21. Kollef MH, Hamilton CW, Ernst FR. Economic impact of ventilator-associated pneumonia in a large matched cohort. Infect Control Hosp Epidemiol 2012; 33(3): 250-6.
22. Dudeck MA, Horan TC, Peterson KD, et al. National Healthcare Safety Network (NHSN) Report, data summary for 2010, device associated module. Am J Infect Control 2011; 39(10): 798-816.
23. Azizi F, Hatami H, Janghorbani M. Epidemiology and control of common disorders in Iran. 2nd ed. Tehran, Iran: Khosravi Publications; 2004. p. 22-6. [In Persian].
24. Aly NY, Al-Mousa HH, Al Asar el SM. Nosocomial infections in a medical-surgical intensive care unit. Med Princ Pract 2008; 17(5): 373-7.
25. Chawla R. Epidemiology, etiology, and diagnosis of hospital-acquired pneumonia and ventilator-associated pneumonia in Asian countries. Am J Infect Control 2008; 36(4 Suppl): S93-100.
26. Ibrahim EH, Ward S, Sherman G, Kollef MH. A comparative analysis of patients with earlyonset vs late-onset nosocomial pneumonia in the ICU setting. Chest 2000;117(5):1434-42.
27. Giard M, Lepape A, Allaouchiche B, et al. Early- and late-onset ventilator-associated pneumonia acquired in the intensive care unit: comparison of risk factors. J Crit Care 2008;23(1):27-33.