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KLİNİK ARAŞTIRMA *Mikrobiyoloji*

Etiology, incidence and risk factors of ventilator associated pneumonia in a training and research hospital intensive care unit in Istanbul

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SUMMARY

In this prospective study, we aimed to identify the factors associated with the development of ventilator- associated pneumonia (VAP) and examine the etiology, and incidence of VAP. Between November 2007 and June 2008, 148 patients who required mechanical ventilation for longer than 48 hours were evaluated. VAP was observed in 54 patients (36 %). Mechanical ventilator and VAP utilization rates were 0.87 and 22.88 in 1000 ventilator days, respectively. The most common three microorganisms cultured from tracheal aspirates were Pseudomonas aeruginosa (n=19), Acinetobacter species (n=11) and Staphylococcus aureus (n=10). Of the 21 risk factors evaluated, 7 factors identified were independently associated with VAP (p<0.05): shock, coma (p<0.0006), antibiotic usage for at least 1 month prior to admission (p<0.04), nasogastric tube insertion (p<0.01), invasive procedures such as bronchoscopy, tracheotomy (p<0.0001), reintubation (p<0.017), intubation more than 5 days (p<0.0001), and smoking (p<0.014). Intensive Care Unit (ICU) clinicians should be aware of the risk factors for VAP to minimize the risk of VAP. Also patient care should be individualized, and procedures like bronchoscopy, and reintubation must be performed and followed up cautiously. Besides these, data about the potential microorganisms and resistance of antibiotics to them will guide the empirical therapy.

Key words: *Etiology, incidence, VAP, risk factors, ICU*

ÖZET

İstanbul'da bir eğitim ve araştırma hastanesi yoğun bakım ünitesinde ventilator ilişkili pnömoninin etyoloji, insidans ve risk faktörleri

Bu prospektif çalışmada, VAP gelişimi ile ilgili faktörlerin belirlenmesi ve VAP'ın etyoloji ve insidansının değerlendirilmesi amaçlanmıştır. Kasım 2007 ile Haziran 2008 tarihleri arasında 48 saatten daha uzun sure mekenik ventilator ihtiyacı olan 148 hasta değerlendirilmiştir. Mekanik ventilator kullanım oranı 0,87 ve VAP hızı 1000 ventilatör gününde 22,88 di. Trakeal aspiratlardan en sık izole edilen üç mikroorganizma Pseudomonas aeruginosa (n=19), Acinetobacter species (n=11) ve Staphylococcus aureus (n=10) tu. Değerlendirilen 21 risk faktöründen 7'si bağımsız olarak VAP ile ilişkiliydi (p<0.05): şok, koma (p<0.0006), başvurudan en az bir ay önce antibiyotik kullanmış olmak (p<0.04), nazogastrik tüp varlığı (p<0.01), bronkoskopi, trakeotomi gibi invaziv prosedürler (p<0.0001), reentübasyon (p<0.017), 5 günden uzun süreli entübasyon (p<0.0001), sigara kullanımı (p<0.014). Yoğun Bakım Ünitesi (YBÜ) klinisyenleri VAP riskini azaltmak için VAP'a sebep olabilecek risk faktörlerinin farkında olmalı, hasta bakımı kişiselleştirilmeli, bronkoskopi, reentübasyon gibi prosedürler dikkatle yapılmalı ve takip edilmelidir. Bunların yanısıra, potansiyel mikroorganizmalar ve antibiyotik dirençleri hakkındaki bilgiler ampirik tedavide kılavuz olacaktır.

Anahtar kelimeler: *Etyoloji, insidans, VAP, risk faktörleri, YBÜ*

INTRODUCTION

VAP is associated with significant morbidity and mortality in ICU in Western and Asian countries [1-3]. The mortality rate of VAP can reach 50 % and the incidence of VAP varies from 6 % to 52 % [4,5]. Knowledge of the incidence of nosocomial infections and their associated risk factors may be important in manifestation of effective use of preventive measures [6,7]. Early, aggressive and empirical therapy with broad-spectrum antibiotics targeting at similar pathogens has been associated with a reduction in VAP mortality rates [8,9].

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Despite improvements in the diagnosis, treatment and prevention of VAP, it remains an important cause of hospital morbidity and mortality [10]. This study is established to determine the etiology and incidence of VAP and to identify the main risk factors for the development of VAP in our ICU population.

PATIENTS and METHODS

Goztepe Training and Research Hospital has 16 beds in ICU run by the Anaesthesiology Department.

Patients who stayed more than 48 hours in ICU were included in the study. Study patients were prospectively followed for the development of VAP during their stay in ICU. The second episodes of VAP were evaluated. VAP was diagnosed according to the standard definitions of the CDC. An infectious disease physician followed all the patients and collected data. Information of each patient was recorded on two standardized forms. First form included age, gender, length of ICU stay, primary reason for ICU admission, underlying diseases, second form included 21 risk factors as underlying lung disease, shock-coma, origin (ethnicity?) of patients, antibiotic usage for at least 1 month prior to admission, diabetes mellitus, renal failure, immunosupression, sedative medication, corticosteroid therapy, H2 receptor blocker usage, nasogastric tube, history of invasive procedure such as bronchoscopy-tracheotomy, reintubation, intubation more than 5 days, frequency of changing the location of the bed, abdominal surgery, cranial surgery, thorax surgery, gastric aspiration, smoking, and frequency of exchanging the breathing circuit before 48 hours.

All the study patients were followed up for the presence of 21 risk factors. Mechanical ventilator utilization rate: ventilator day/patient-day, VAP incidence rate in 1000 days of ventilation was calculated as VAP/patient-day x 1000. Bacterial isolates were identified by infectious disease specialists. After the first step tests like the gram stain test, coagulase and catalase tests (BBL Crystal Identification Systems, GP-E/NF, Becton Dickinson, USA) were used for identification of microorganisms. Antibiotic susceptibilities were assessed by means of Kirby-Bauer disc diffusion method according to the standards of Clinical and Laboratory Standards Institute (CLSI).

Graphpad 4.0 and SPSS 11.0 were used in statistical analysis. For the comparisons among groups chi-square and Fischer's *chi*-square, for the significance of the groups 1/1, ½ and 2/2 univariate analysis and for multiple comparisons Tukey's range test were used. $p<0.05$ was accepted as statistically significant.

RESULTS

In a 7 month-study period (November 2007-June 2008) a total of 276 patients were admitted to the ICU. 148 patients who required mechanical ventilation for longer than 48 hours were evaluated. Of 148 patients 85 were men (57.4 %), and 63 were women (42.6 %). VAP occurred in 54 patients (36 %). Mean age of VAP (+) and VAP (-) patients were 47.48±24.09, and 42.9±26.49 years, respectively. Length of stay of VAP (+) group was 28.25±27.72 days and 8.36±7.14 days in VAP (-) group. Mortality rates were 51.9 % (n=28) in VAP (+) and 34 % (n=32) in VAP (-) patients.

Mechanical ventilator utilization rate was 0.87, VAP rate in 1000 ventilator days was 22.88. VAP developed within a mean of 10.32 days. There were 65 episodes of VAP in 54 patients. Of 65 episodes, 11 of them had multiple microorganisms (16.9 %). The most common three organisms cultured from tracheal aspirates were *Pseudomonas aeruginosa* (n=19), *Acinetobacter species* (n=11) and *Staphylococcus aureus* (n=10). The resistance of *Pseudomonas aeruginosa* to various antibiotics were as follows; imipenem 42.1 %, ciprofloxacin 26.3 %, piperacillin-tazobactam 26.3 %, ceftazidime 52.6 %. The rate of resistance of *Acinetobacter*

species to imipenem was 27.3 % and the rate of resistance of *Staphylococcu aureus* to oxacilline was 80 %. Within the first five days *Pseudomonas aeruginosa* (n=6), *Escherichia coli* (n=5), *Staphylococcus aureus* (n=2) and in the following days *Pseudomonas aeruginosa* (n=13), *Acinetobacter species* (n=9), *Staphylococcus aureus* (n=8) were isolated. The risk factors significantly correlated with the development of VAP were shock-coma, antibiotic usage for at least 1 month prior to admission, nasogastric tube, bronchoscopy-tracheotomy, reintubation, intubation more than 5 days, and smoking (Table 1). There was no significance correlation between VAP and the other 14 risk factors (Table 2).

Table 1. Variables independently associated with ventilator-associated pneumonia.

Variable	VAP (n=54)	Non VAP (n= 94)	P
Shock-coma	45	52	0.0006
Antibiotic usage	13	11	0.04
Nasogastric tube	50	72	0.01
Bronchoscopy/tracheotomy	24	10	0.0001
Reintubation	22	21	0.017
Intubation more than 5 days	36	24	0.0001
Smoking	25	25	0.014

Table 1. Variables independently associated with ventilator-associated pneumonia.

Variable	VAP (n=54)	Non VAP (n= 94)	P
COPD*	11	31	0.101
Origin of patient	23	51	0.17
Diabetes mellitus	4	13	0.57
Renal failure	3	3	0.40
Immunosupression	2	8	0.32
Sedative medication	43	67	0.26
Corticosteroid therapy	19	24	0.21
H2 receptor blocker usage	44	76	0.92
Changing the location of the bed	18	19	0.07
Abdominal surgery	10	21	0.58
Cranial surgery	17	23	0.35
Thorax surgery	1	3	0.61
Gastric aspiration	3	1	0.13
Exchanging the breathing circuit	15	24	0.76

**COPD: Chronic Obstructive Pulmonary Disease*

DISCUSSION

VAP has been noted as the most common nosocomial infection and represents a major threat to all ICU patients. The incidence of VAP in our study was high, 22.8 VAPS/1000 ventilator-days, compared with rates based on NNIS (5.4), and INICC (10.4) data [11,12]. Higher rates of VAP observed in our group may be due to increased frequency of mechanical ventilation performed compared to other studies. Mechanical ventilator utilization rate was recorded as 0.87 in the study group, 0.37 and 0.26 in NNIS and INICC data, respectively. Most of the ICU population in the study consisted of traumatic brain injury and multiple trauma patients. In the analysis of NNIS data, it was observed that with the increase number of trauma patients, mechanical ventilation requirement and in neurointensive care units VAP incidence were increased [11]. In the study of Giard et al the most frequently isolated VAP pathogens were *Staphylococcus aureus* (20.4 %) and *Pseudomonas aeruginosa* (17.8 %) [13]. In this study as in the study of Magnason et al gram- negative bacilli were the mostly isolated pathogens and *Staphylococcu aureus* ranked the third in dominancy [14]. Katherason et al have also cultured gram negative bacilli such as *Klebsiella pneumoniae*, *Acinetobacter species* and *Pseudomonas aeruginosa* [1].

In a study published in Brazil imipenem resistant *Pseudomonas aeruginosa* (52.0 %), and *Acinetobacter baumannii* (11.0 %), and oxacillin resistant *Staphylococcus aureus* (65.4 %) were isolated in respective percentages [15]. The resistance rates determined in this study group differed largely from the results of the study of Rocha et al from Brazil. In Rocha's study imipenem resistance of *Pseudomonas aeroginosa* was lower, but of *Acinetobacter species* was two- fold higher, oxacilin resistance of *Staphylococcus aureus* was also very high. There is a two- year- interval between this and Rocha's studies and in these two years there has been a great variance in resistance range of VAP microorganisms in the world.

Early and late-onset VAP have been compared in two studies and it has been concluded that late-

onset VAP has been associated with longer mechanical ventilation duration and pathogens isolated were more resistant [13,16]. In our patients with early-onset VAP, *Escherichia coli* was the second pathogen and with late VAP, *Acinotobacter species* was isolated with a high resistance potential.

In this study, the the most frequently isolated pathogen microorganisms of early and late-onset VAP maintained its first and third row, but the second row changed. The limitation of this study is that the antibiotic resistance of microorganisms isolated in early and late-onset VAP was not given. However, detection of microorganisms with a potential for higher resistance rates such as Acinetobacter species which is the second common cause in late-onset VAP and has a higher resistance profile as indicated in other studies supports the above-mentioned studies.

The top risk factors associated with VAP were the consciousness of the patient (shock-coma), invasive procedures (bronchoscopy, tracheotomy) and intubation of more than 5 days. Apostolopoulou and Ibrahim have also reported bronchoscopy and tracheotomy as risk factors for VAP [17,18]. Bronchoscopy being a risk factor may force the microorganisms colonized in upper airway to migrate to lower respiratory tract or the patient to whom bronchoscopy is performed already has atelectasia and intensive secretions. Detailed investigations may be needed for this difference. Tracheotomy and leakage around the endotracheal tube cuff and resultant pooled secretions might lead to VAP [19].

In a study from Malaysia it was stated that a shorter period of mechanical ventilation had significantly reduced the incidence of VAP and every one day had increased the rate of the development of VAP by about 4 % [1]. In this study, it is possible to see the significant difference in the duration of hospital stay between VAP (+) and VAP (-) groups of patients.

Antibiotic usage for at least one month prior to admission, enteral nutrition via nasogastric tube and reintubation are the critical risk factors associated with VAP similar to the ones reported in the literature [5,18,20-23]. A remarkable difference of this study from the literature is that the presence of chronic obstructive pulmonary disease and antacid medication were independent risk factors for VAP, which may be related to a few number of chronic obstructive pulmonary disease patients. Magnason et al also reported that antacids were not risk factors for VAP and colonized microorganisms in trachea and stomach were of distinct strains and assumption of the migration of microorganisms from stomach to trachea was not supported [14].

This study is the first one which identified smoking history as an independent risk factor for VAP.

CONCLUSION

Determination of risk factors, causative organisms and patterns of resistance will ensure the reduction of VAP rate and initiation of fast and effective antibiotic therapy which is the most important factors effecting improved survival. The continuity of such studies would be appropriate for the consideration of possible changes in risk factors, variety of microorganisms and antibiotic resistance over time.

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