Göztepe Tıp Dergisi 28(1):14-18, 2013
doi:10.5222/J.GOZTEPETRH.2013.014

ISSN 1300-526X

KLİNİK ARAŞTIRMA *Microbiology*

Etiology, incidence and risk factors of ventilator associated pneumonia in an intensive care unit of a training and research hospital 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 utilizationrate was 0.87, and VAP rate in 1000 ventilator days was 22.88. The most common three microorganisms cultured from tracheal aspirates were Pseudomonas aeruginosa (n=19), Acinetobacter spp.(n=11), and Staphylococcus aureus (n=10). Of the 21 risk factors evaluated, 7 factors identified were independently associated with VAP (p<0.05) such as 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 lasting for 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, patient care should be individualized, and procedures like bronchoscopy, reintubation must be performed and followed up cautiously. Besides these, data about the potential microorganisms and those resistant to antibiotics 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 mekanik 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*

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 for the 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].

Despite improvements in the diagnosis, treatment and prevention of VAP, it remains an important cau-

Geliş tarihi: 24.08.2012
Kabul tarihi: 13.12.2012
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se 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, and second episodes of VAP were evaluated. VAP was diagnosed according to the standard definitions of the CDC. A specialist in infectious diseases monitored all study patients and collected relevant 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 of patients, antibiotic usage for at least 1 month prior to admission, diabetes mellitus, renal failure, immunosupression, sedative , and/or corticosteroid therapy, H2 receptor blocker usage, nasogastric tube, invasive procedure such as bronchoscopy-tracheotomy, reintubation, intubation more than 5 days, changing the location of the patient's bed, abdominal, cranial, thoracal surgery, gastric aspiration, smoking, exchanging the breathing circuit at intervals shorter than 48 hours.

All the study patients were followed up for the presence of 21 risk factors. Mechanical ventilator utilization (ventilator day/patient day), and VAP incidence rates in 1000 days of ventilation were calculated based on the formula: VAP/patient day X 1000. Bacterial isolates were identified by infectious disease specialists. After the first step tests like the gram stain test, coagulase test and catalase test (BBL Crystal Identification Systems, GP-E/NF (Becton Dickinson, ABD) were used for the 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 comparison of the 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 significant.

RESULTS

In a 7- month- study period (November 2007-June 2008) a total of 276 patients were admitted to the ICU, and 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 rate was 51.9 % (n=28) in VAP (+) and 34 % (n=32) in VAP (-) patients.

Mechanical ventilator utilization rate was 0.87, and VAP rate in 1000 ventilator days was 22.88. VAP was developed with a mean of 10.32 days. There were 65 episodes of VAP in 54 patients. Of the 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 rates of antibiotic resistance of *Pseudomonas aeruginosa* were as follows; imipenem 42.1 %, ciprofloxacin 26.3 %, piperacillin-tazobactam 26.3 %, and ceftazidime 52.6 %. The rate of resistance of imipenem for *Acinetobacter species* was 27.3 % and the rate of resistance of oxacilline for *Staphylococcus aureus* was 80 %. *Pseudomonas aeruginosa* (n=6), *Escherichia coli* (n=5), *Staphylococcus aureus* (n=2) were isolated during the first five, and *Pseudomonas aeruginosa* (n=13), and *Acinetobacter species* (n=9), *Staphylococcus aureus* (n=8) in the following days.

The risk factors that have significant correlation with the development of VAP were shock-coma, antibiotic usage for at least 1 month prior to admission, nasogastric tube, bronchoscopy-tracheotomy, reintubation, intubation lasting for more than 5 days, and smoking (Table 1). There was no significant 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 2. Variables not significantly 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 was noted as the most common nosocomial infection and represents a major threat to all ICU patients. The incidence of VAP in our study was relatively higher (22.8 VAPS/1000 ventilator days) considering the corresponding rates reported by NNIS (5.4), and INICC (10.4) [11,12]. These higher rates of VAP observed in our group may be due to the relatively increased application of mechanical ventilation in our ICU unit.. Mechanical ventilator utilization rate was recorded as 0.87 in the study group, 0.37 and 0.26 in NNIS and INICC 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 in the number of trauma patients, mechanical ventilation requirement and VAP incidence in neurointensive care units also 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 mostly isolated and Staphylococcu aureus was the third one in dominancy [14]. Katherason et al have also cultured gram negative bacilli such as *Klebsiella pneumonia, Acinetobacter species* and *Pseudomonas aeruginosa* [1].

In a study published in Brazil imipenem resistant *Pseudomonas aeruginosa* (52.0 %), imipenem resistant *Acinetobacter baumannii* (11.0 %), oxacillin resistant *Staphylococcus aureus* (65.4 %) were isolated in respective rates [15]. The resistance rates determined in this study group differed largely from the results of the study of Rocha et al from Brazil; imipenem resistance of *Pseudomonas aeroginosa* was lower, while of *Acinetobacter species* was two folds higher. However, oxacilin resistance of *Staphylococcus aureus* was 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 VAP has been associated with longer mechanical ventilation and the pathogens isolated in late VAP were more resistant [13,16]. In our patients with early VAP, *Escherichia coli* was the second pathogen in effectiveness and with late VAP, *Acinotobacter species* isolates had a higher resistance potential.

In this study, pathogenic microorganisms ranking

first, and third among culprit isolates of early and late VAP remained the same, but the second most common isolate changed. However as a limitation of this study, the antibiotic resistance of microorganisms isolated in the early and late VAP was not indicated. However, as the second common causative agent in late VAP, the detection of *Acinetobacter species* which potentially have a higher resistance rate, and its higher resistance profile indicated in other studies, support 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 lasting more than 5 days. Apostolopoulou and Ibrahim have also reported bronchoscopy and tracheotomy as a risk factor for VAP [17,18]. Bronchoscopy being a risk factor may force the microorganisms colonized in the upper airway to migrate to the lower respiratory tract . Bronchoscopy is also contraindicated in patients who had already atelectasia and intensive bnronchopulmonary secretions. Detailed investigations may be needed on this issue. Tracheotomy and leakage around the endotracheal tube cuff lead to VAP because of further accumulation of pooled secretions [19].

A study from Malaysia indicated that a shorter period of mechanical ventilation significantly reduce the incidence of VAP and each extra day in mechanical ventilation increase the probability of the development of VAP 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 are independent risk factors for VAP in a small number of chronic obstructive pulmonary disease patients. Magnason et al have also reported that antacids are not risk factors for VAP. They also stated that colonized microorganisms in trachea and stomach are distinct strains and assumption of the migration of microorganisms from stomach to trachea is not supported by robust evidence [14].

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

CONCLUSION

Determination of risk factors, causative organisms and patterns of resistance will provide the reduction of VAP rate and enable to start on a fast and effective antibiotic therapy which is the most important factors of survival. The continuity of such studies would be appropriate in consideration of possible changes in the risk factors, variety of microorganisms and antibiotic resistance over time.

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