Original Article

A Study of Ventilator-Associated Pneumonia in King Narai Hospital†

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Objective: 1) Determine the ventilator-associated pneumonia (VAP) occurrence rate, duration time to develop VAP, the microorganisms causing VAP, and mortality rate of VAP patients. 2) Analyze the factors related to VAP among patients' characteristics, underlying diseases, and APACHE II score. 3) Analyze the risk factors to VAP and risk factors that cause death in VAP patients.

Materials and Methods: A prospective observational study of patients aged more than 15 years, who were on a mechanical ventilator for more than two calendar days, hospitalized at King Narai Hospital, Lopburi Province, Thailand between April and July 2016. Data were analyzed through descriptive and inferential statistics using an SPSS program.

Results: Among the 307 patients that underwent mechanical ventilation for more than two calendar days, 169 patients were male (55.05%). The mean age was 61.74 years (SD 18.42). Patients with DM, IHD or CHF, CKD, COPD, and CVA were 23.78%, 14.66%, 10.75%, 9.45%, and 8.14%, respectively. The mean APACHE II score was 19.34 (SD 5.15). Out of 307 patients, 88 cases (28.7%) developed VAP. The incident rate was 13.65 occurrences per 1,000 days. The mean duration time for VAP was 10.52 days (SD 8.23). The mean ventilation days were 18.43 (SD 15.98). The majority of VAP or 72 cases (69.32%) was caused by *Acinetobacter baumannii* XDR, which was pan drugs-resistant and resisted to all antibiotic groups except tigecyclin and colistin, resulting in the death of 62.5% of VAP patients. If analyzed in all intubated groups, the mortality rate from VAP was 17.9% in all patients that received mechanical ventilation. The risk factors for VAP, which was statistically significant at *p*-value smaller than 0.01, were treated with nebulizer, duration time on ventilator, drowsy, and semi-coma patients. At *p*-value smaller than 0.05 were APACHE II score, stuporous patients, senility, or bed ridden patients.

Conclusion: The incident rate of VAP in King Narai Hospital was 13.65 occurrences per 1,000 days, and the mortality rate from VAP was 62.5%. The majority of VAP (69.32%) was caused by *A. baumannii* XDR. The significant risk factors that had effect on mortality from VAP were treated with nebulizers, the duration time on the ventilator, high APACHE II score, consciousness condition (stupor and semi-coma).

Keywords: Ventilator associated pneumonia (VAP), Risk factor, APACHE II score, King Narai Hospital

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Ventilator-associated pneumonia (VAP) is a type of lung infection that occurs in people who are on a mechanical ventilation in hospitals. As such, VAP typically affects critically ill people in an intensive care unit (ICU). VAP is a major source of increased illness and death[1]. In United States of America, the infection control unit in hospitals found a VAP infection rate of 15% and the mortality rate for VAP had been cited to be 42.5%[2]. A study in Europe found that one half of all causes of hospital infections in critical ill patients were due to VAP[3], and it was a risk factor that caused death. Patients receiving mechanical ventilation had 20 times higher rate of becoming affected by VAP than those who did not. Patients who were administered an endotracheal tube and received mechanical ventilation were the high-risk group for development of VAP. The study found the length of the VAP occurrences to be from 10% to 25% of all patients receiving a mechanical ventilation[4]. The mortality rate of the VAP patients in a hospital was 20% to 50%[5]. The factors associated to VAP were those concerning the patients' characteristics, nutrition status, comorbidity diseases, severity of the illness, immunological status, as well as factors related to pathogens, endogenous or exogenous sources, factors related to environment, contact from medical personnel, technical use of a mechanical

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ventilator, care of a ventilator circuit, and medical use of a nebulizer and humidifier[6]. The VAP also had an impact on the patients' management and length of hospital stay. These factors were usually attributed to making the case became more complicated, resulting in multiple drug resistance (MDR) and costly treatment[7] with an increase length of hospitalization and death.

The objectives of the present study were to 1) determine the VAP occurrence rate, duration of VAP, and mortality rate of VAP patients, 2) analyze the factors related to VAP, patients' characteristics, underlying diseases and patients APACHE II score, 3) determine microorganisms that cause VAP and drug sensitivity, and 4) analyze the risk factors to VAP occurrence and risk factors that cause death in VAP patients.

Materials and Methods

A prospective observational study was conducted on patients aged over 15 years receiving a mechanical ventilation for more than two calendar days in King Narai Hospital. The inclusion criteria were all ventilated patients on mechanical ventilation for more than two calendar days. The exclusion criteria were patients who developed pneumonia before using mechanical ventilation or patients with pneumonia after removal of mechanical ventilation more than two calendar days. Data were collected from in-patient' medical records between April and July 2016. The eligible patients were carefully followed up for developing VAP by monitored the signs and symptoms, change in the chest X-ray, and sputum culture report. The diagnosis of VAP was based on criteria from the Centers for Disease Control and Prevention (CDC) and National Healthcare Safety Network (NHSN)[8]; such as, at least one of the following symptoms, fever greater than 38°C, leukocytosis at 12,000/mm³ or more, leukopenia less than 4,000/mm³, or altered mental status in aging older than 70 years. At least two of the following signs detected, new onset of purulent sputum or change in character, new onset of worsening cough or dyspnea or tachycardia, rales or bronchial breathing sound, or worsening blood gas. Abnormality of the chest X-ray displayed at least one of the following, new or progressive and persistent infiltration and consolidation changed. The laboratory report mentioned at least one of the following, positive blood culture not related to another infection, positive pleural fluid culture, or positive quantities from minimally contaminated lower respiratory tract specimens. The study of the microorganisms causing VAP was conducted from the sputum culture and drug sensitivity, and the severity of the illness was analyzed by using an APACHE II score[9]. The follow up was terminated after removing the mechanical ventilator for more than two calendar days or the patient had died.

Ethical approval

Ethical approval was obtained from the Ethics Committee of the King Narai Hospital before the research was conducted.

Statistical analysis

All statistical analyzes were performed using SPSS version 11.5 (SPSS Inc., Chicago. Illinois, USA). The sample size estimation is important in medical applications, especially in logistic regression. One guideline suggest that there should be 10 patients per independent variable (Vittinghoff and McCulloch, 2007)[10]. In the present study, the sample size was 307 for 5 predictors, it should be acceptable to get high statistical power. Data were analyzed through descriptive statistics (frequency, percentage, mean and standard deviation; SD) for all variables concerning the patients' characteristics, the environment, micro-organisms, and medication. Inferential statistics were applied using a Chi-square test for association between the categorical variables, and multivariate logistic regression was utilized for identifying the risk factors of the VAP occurrence and death from VAP.

Results

A prospective observational study was conducted on patients aged over 15 years receiving a mechanical ventilation for more than two calendar days between April and July 2016 in King Narai Hospital. The sample comprised of 307 patients, 161 males (55.01%) and 138 females (44.95%).

The age of the studied patients were 71 to 80 years in 70 cases (22.80%), 51 to 60 years in 57 cases (18.57%), 61 to 70 years in 56 cases (18.24%), 81 to 90 years in 46 cases (14.98%), 41 to 50 years in 31 cases (10.10%), and the mean age was 61.74 years (SD 18.42). Percentage of comorbidity of the studied patients were diabetes mellitus (DM) in 73 cases (23.78%), ischemic heart disease (IHD) or congestive heart failure (CHF) in 45 cases (14.66%), chronic kidney disease (CKD) in 33 cases (10.75%), chronic obstructive pulmonary disease (COPD) in 29 cases (9.45%), cerebrovascular accident (CVA) in 25 cases (8.14%), malignancy in 22 cases (7.17%), alcoholism in 18 cases (5.86%), cirrhosis in 16 cases (5.21%),

senility in 14 cases (4.56%), and bed ridden in 11 cases (3.58%).

Severity of illness assessed by APACHE II score were 15 to 19 (40.07%), 20 to 24 (27.36%), 25 to 29 (14.66%), and 10 to 14 (12.38%). The mean APACHE II score was 19.34 (SD 5.15).

Duration of receiving a mechanical ventilation in the studied patients were 3 to 7 days in 88 cases (28.66%), 8 to 14 days in 85 cases (27.69%), 15 to 12 days in 41 cases (13.36%), and 22 to 28 days in 29 cases (9.45%). Mean ventilator days was 18.43 days (SD 15.98).

The studied patients were admitted in medical ward in 164 cases (53.42%), ICU of surgery in 80 cases (26.06%), ICU of medicine in 42 cases (13.68%), surgical ward in 14 cases (4.56%), and orthopedic ward in four cases (1.30%).

All the patients were prevented for developing VAP by following the guideline recommendation of CDC and the Health Infection Control Practice Advisory Committee in prevention of contact with contaminated hand by healthcare personnel, oropharyngeal cleaning with 0.12% chlorhexidine gluconated, semi-upright position, drainage of subglottic secretion, monitor pressure cuff of endotracheal tube, care of breathing circuit, and heat moisture exchange.

Table 1. The cause of using a mechanical ventilator in studied patients (n = 307)

	n (%)
CHF or IHD	62 (20.19)
Sepsis, septic shock	57 (18.57)
COPD	38 (12.38)
ICH or CVA	37 (12.05)
Head injury	36 (11.73)
Trauma	24 (7.82)
Post operation	14 (4.56)

CHF = congestive heart failure; IHD = ischemic heart disease; COPD = chronic obstructive pulmonary disease; ICH = intracerebral hemorrhage; CVA = cerebrovascular accident

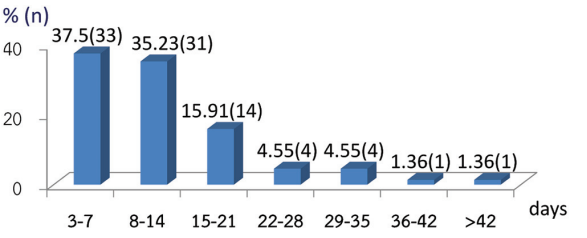

Figure 1. Duration of mechanical ventilator before VAP developed in the studied patients (n = 88).

Fifty-nine cases received major operation, which included 34 cases in neurosurgery, six cases of thoracic surgery, and 13 cases of abdominal surgery.

The present study found 88 cases of the patients developed VAP (28.66%). The incidence rate of VAP was 13.65 occurrences per 1,000 days.

Mean duration of mechanical ventilator before VAP developed was 10.52 days (Figure 1).

The multivariate logistic regression of the factors affecting the occurrence of VAP revealed that patients using a nebulizer had a significant *p*-value smaller than 0.01, while those receiving a proton pump inhibitor, steroids, sedative drug, and inhaler use were not statistically significant (Table 2). Previous studies showed that using a nebulizer or inhaler provided a normal result but using an inhaler cost less[11].

Abnormality of chest X-ray in the present study were bilateral infiltration 43.18%, right lower lobe (RLL) infiltration 39.77%, left lower lobe (LLL) infiltration 22.73%, interstitial infiltration 9.09%, left upper lobe (LUL) infiltration 4.55%, and right upper lobe (RUL) infiltration 3.41%.

The most common pathogens that caused VAP was *Acinetobacter baumannii* XDR (69.32%). The other pathogens were *Pseudomonas aeruginosa* (11.36%), *Klebsiella pneumoniae* (ESBL) (5.68%), *Stenotrophomonas maltophilia* (5.68%), *P. aeruginosa*

Table 2. Risk factors affecting the occurrence of VAP (n = 307)

Factor	VAP (n = 88), n (%)	Non VAP (n = 219), n (%)	Total (n = 307), n (%)	*p*-value	OR	95% CI
Receiving a proton pump inhibitor	58 (65.91)	116 (52.97)	174 (56.68)	0.396	0.488	0.21 to 1.78
Receiving steroids	16 (18.18)	24 (10.96)	40 (13.03)	0.566	0.358	0.22 to 1.41
Receiving a nebulizer and/or inhaler	26 (29.55)	50 (22.83)	76 (24.76)			
Nebulizer only	12 (13.64)	13 (5.94)	25 (8.14)	0.001**	4.864	2.71 to 9.42
Inhaler only	5 (5.68)	25 (11.42)	30 (9.77)	0.616	0.762	0.24 to 1.32
Nebulizer and inhaler	9 (10.23)	12 (5.48)	21 (6.84)	0.011*	4.241	2.02 to 8.27
Receiving sedative drug	19 (21.59)	37 (16.89)	56 (18.24)	0.916	0.283	0.13 to 1.18

VAP = ventilator-associated pneumonia; OR = odds ratio; CI = confidence interval

* $p<0.05$, ** $p<0.01$

Table 3. Risk factors effecting VAP and deaths from VAP in the studied patients

Risk factors	VAP	Deaths from VAP		
	p-value	*p*-value	Adjusted OR	95% CI
Time on an endotracheal tube	0.001**	0.001**	2.062	1.037 to 2.088
APACHE II score	0.029*	0.049*	2.096	1.004 to 2.196
Nebulizer	0.001**	0.014*	3.208	1.272 to 8.091
Consciousness				
Level 1 (drowsiness)	0.001**	0.171	0.839	0.318 to 2.210
Level 2 (stupor)	0.959	0.011**	4.894	1.443 to 16.604
Level 3 (semicoma)	0.323	0.002**	4.857	1.817 to 12.983
Bedridden	0.476	0.032*	1.592	1.102 to 2.259

VAP = ventilator-associated pneumonia; OR = odds ratio; CI = confidence interval

* $p<0.05$, ** $p<0.01$

(MDR) (4.55%), and *Escherichia coli* (ESBL) (4.55%). In terms of drug sensitivity, *A. baumannii* XDR showed a pattern of resistance to all drug groups, except tigecycline and colistin.

Level of consciousness in the studied patients, mostly were good consciousness (level 0) in 56.03%, drowsiness (level 1) in 22.43%, stupor (level 2) in 17.92%, and semi-coma (level 3) in 3.58%. Outcomes of treatment in the studied patients found death from VAP in 55 cases (17.91%), death from other causes in 68 cases (22.15%), and discharged in 176 cases (57.33%).

The multivariate logistic regression of the factors affecting VAP revealed the time on ventilator, use of a nebulizer, and consciousness level 1 (drowsiness) had significant *p*-value of less than 0.01, as high APACHE II score showed significant *p*-value of less than 0.05. Table 3 also showed the factors affecting the deaths from VAP, time on a ventilator, and consciousness level 3 (semi-coma) had a significant *p*-value of less than 0.01, as the APACHE II score, use of a nebulizer, bedridden, and consciousness level 2 (stupor) had a significant *p*-value of less than 0.05. As can be seen, the time on a ventilator, APACHE II score, and use of a nebulizer were crucial risk factors for both the occurrence of VAP and deaths from VAP.

Discussion

For the present study, out of 307 mechanically ventilated patients, 88 patients (28.66%) were diagnosed with VAP. The incidence was 13.65 occurrences per 1,000 ventilator days. A previous study conducted by Danchaivijitr et al (2005)[12] found 12.60 occurrences per 1,000 ventilator days and an epidemiology study in 42 hospitals in Thailand[13] also found that the VAP rates ranged between 11.50 and 14.30 per 1,000 ventilator days. The 307 mechanically ventilated patients had a mean (SD) of 61.74 (18.42) years. The common comorbidity disease among patients were DM (23.78%), IHD/CHF (14.66%), CKD (10.75%), and COPD (9.45%). The higher age groups were a risk factor due to their decreased immune status; therefore, there was an increase in illness and severity conditions. The APACHE II score ranged during 15 to 19 (40.07%), 20 to 24 (23.36%), and the mean APACHE II score and standard deviation were 19.34 and 5.15, respectively. The present study found a positive relationship between the APACHE II score and the mortality rate. This was in accordance with a prior study conducted by Klompas et al (2014)[14]. In the present studied, the patients were admitted in medical ward in 67.1%, and the surgical ward in 31.92%. Fifty-nine cases received major operation, which was neurosurgery in 34 cases. The major causes of mechanical ventilator were CHF or IHD in 20.19%, sepsis in 18.57%, and COPD, CVA or ICH, and head injury in 12.38%, 12.05%, and 11.73%, respectively. The patients' days on a ventilator had a mean (SD) of 18.43 (15.98) days, and the time on the ventilator was associated with the occurrence of VAP. In a large cohort study, Wunsch et al (2010) [2] found that the estimated risk was 3% per day in the first week, 2% per day in the second week, and 1% per day in the third week. The present study found that the majority of VAP occurrence was during 3 to 7 days (37.50%) and 8 to 14 days (35.23%). The risk was greatest during the first seven days of the mechanical ventilation, which was in accordance with a prior study conducted by Giantsou et al (2005)[15] that found VAP mostly occurred in 5 to 7 days. Furthermore, the present study found that the use of a nebulizer had a significant effect on VAP while the use of an inhaler had no effect. The findings were consistent with the study conducted by Ehrmann et al (2013)[16], which found that using a nebulizer could distribute bacteria into

the lower respiratory tract through an aerosol route by contacting with contaminated respiratory equipment. Moreover, the empirical data showed that the use of an inhaler cost less than the use of a nebulizer while both gave the same efficiency[17]. The present study revealed these factors (patients receiving a proton pump inhibitor, steroids, and sedative drugs) did not show any significant on VAP occurrence differences from prior studies[18,19].

In general, the sensitivity of a chest X-ray for the diagnosis of VAP was low (25%), the specificity of new or worsening infiltration was 50% to 78%, and signs of air bronchograin was 58% to 83%[20]; however, information from a CT scan would increase the efficiency of detecting VAP by adding 26%[21]. In the present study, examination of new or progressive infiltration on a chest X-ray showed that the bilateral infiltration to be 43.18%, RLL infiltration at 39.77%, and LLL infiltration 22.73%.

The most common pathogens from the sputum culture was *A. baumannii* XDR (69.32%), which was a multiple drug resistant organism. The pattern of the drug sensitivity showed resistance in all antibiotic groups except tigecycline and colistin, which were endemic organisms in the hospital that limited the choice of the antibiotic treatment in the hospital and placed the attributable mortality from VAP up to 62.5% in all VAP patients. In contrast, the study of Klompa et al (2013)[22] found that the mortality in the VAP patients was 18% to 48%. From the overview of the intubated patients, the present study showed the mortality rate from VAP 17.91% in all intubated group, which was in accordance with a study conducted by Melsen et al (2013)[23] that found the mortality rate from VAP to be between 8% to 28% in all intubated patients.

The duration time on a ventilator was a risk factor for the development of VAP ($p<0.01$). It was found that ventilated patients for longer duration were more susceptible than those with shorter duration[24]. Furthermore, patients received an inhaler showed no significant effect from VAP, but those used nebulizer did. Consciousness patients with drowsiness were also susceptible to VAP[25]. In addition, the APACHE II score was found to be a risk factor of VAP ($p<0.05$).

The risk factor of mortality in VAP patents with a *p*-value smaller than 0.01 was the duration time on a ventilator, especially consciousness patients in a semi-coma condition. The risk factors of mortality in VAP patients with a *p*-value smaller than 0.05 were the APACHE II score, consciousness patients in a stupor, and those in a bedridden status. The consciousness factor was a crucial risk factor, as patients who were drowsy, stupor, and semi-coma had a significant effect on VAP occurrence. This was due to reduce effectiveness of clearing secretion in the oropharynx, a defense mechanism, led to aspirate the secretion. Similarly, patients who were bedridden led to easily aspirated and developed pneumonia.

Conclusion

Among the 307 patients receiving mechanical ventilation, 88 patients developed VAP (28.66%). The incidence of VAP was 13.65 occurrence per 1,000 ventilation days. The most common pathogen was *A. baumannii* XDR (69.32%), caused a mortality rate of 62.5% in VAP patients. The significant risk factors on VAP were the duration of time on the ventilator, nebulizer treatment, APACHE II score and consciousness condition (stupor and semi-coma), which influenced mortality. Therefore, patients' consciousness should be considered. The selective use of an inhaler instead of a nebulizer should be considered as well. The hospital healthcare personnel should follow the "VAP bundle"[26], try to use early extubation, take into account the patients' consciousness condition and bedridden status.

What is already known on this topic?

The factors associated to VAP included the patients' medical conditions, comorbidity diseases, nutritional status, immune suppression, severity of illness, level of consciousness, body position, factors related to environment, contact from medical personnel such as inadequate hand hygiene, technical use of a mechanical ventilator, and care of a ventilator circuit. The duration time on ventilator were major cause of developed to VAP.

What this study adds?

In the present study, the authors found that nebulizer treatment was a risk factor for development of VAP, while the use of an inhaler had no effect. Consciousness status such as the drowsiness condition, and a high APACHE II score were risk factor to VAP. The study found that a consciousness condition (stupor and semi-coma) affected mortality from VAP.

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Potential conflicts of interest

The authors declare no conflict of interest.

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