Incidence and Risk Factors for Ventilator-Associated Pneumonia in Kathmandu University Hospital

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ABSTRACT

Background

Ventilator associated pneumonia is a major cause of morbidity in the intensive care unit. Difficulties in identification of the risk factors, in diagnosing and in prevention, have intensified the problem.

Objectives

To measure the incidence of ventilator associated pneumonia in intensive care unit and to identify the risk factors associated.

Methods

A prospective observational cohort study of 69 patients who were mechanically ventilated for more than 48 hours were evaluated to find out the development of nosocomial pneumonia and presence or absence of risk factors. Data were subjected to univariate analysis using chi-square and t-test. Level of significance was set at 0.05.

Results

Twenty two (31.88%) out of 69 patients developed ventilator associated pneumonia, majority of them between four days to 14 days. Reintubation, invasive lines, H_2 blockers and low PaO_2/FiO_2 were identified as major risk factors in our study. Enteral feeding via nasogastric tube and use of steroids was not associated with development of ventilator associated pneumonia. The patients with ventilator associated pneumonia had significantly longer duration of mechanical ventilation (18.88±7.7 days vs 7.36±4.19 days) and stay (29±17.8 days vs 9.22±5.14 days). The morality was similar for both the groups with or without ventilator associated pneumonia.

Conclusion

The incidence of ventilator pneumonia is high. Patients requiring prolonged ventilation, re-intubation, more invasive lines and H_2 blockers, are at high risk and need special attention towards prevention.

KEY WORDS

nosocomial infection, prolonged mechanical ventilation, risk factors, ventilator associated pneumonia

INTRODUCTION

Nosocomial infections are common in the Intensive Care Unit (ICU) and ventilator associated pneumonia (VAP) represents second most common nosocomial infection in the ICU.[1] Ventilator associated pneumonia stands as an important cause of hospital morbidity and mortality.[2,3] Intubated patients are at risk of developing VAP and the incidence increases with the duration of ventilator support. The cumulative risk is estimated to be 1%- 3% per day of mechanical ventilation.[4] The incidence varies depending on criteria used for diagnosis, the type of ICU, and hospital resources or study population. Data from developing countries reveal an incidence which ranges from 15.87%-30.67%. [5]

During prolonged mechanical ventilation, the oropharynx, nasopharynx, sinuses and dentition become colonized with pathogens which with secretions get pooled into the subglottic space. These then make their way to the lower respiratory tract via micro-leak in the endotracheal tube cuff, thus causing pneumonia. In addition, the endotracheal tube holds the vocal cords open, further allowing access to the aspirate. Re-intubation, higher APACHE score, multiple invasive lines, immunosuppression, enteral feeding via nasogastric tube, H_2 blockers, antacids, supine head position, paralytic agents and sedation are all independent risk factors for VAP.[6] This prospective study was conducted in a five beded ICU in Dhulikhel Hospital, Kathmandu

University hospital over a period of two and a half years to define the magnitude of this problem by finding out the incidence, common organisms involved and the associated risk factors.

METHODS

This prospective, observational cohort study was undertaken after obtaining approval from hospital Institution Research Committee and written, informed consent form the patients' relatives before putting on ventilator. The study took place in a five beded adult ICU of Dhulikhel Hospital, a 340 beded University Hospital. Over the duration of two and a half years, starting from January 2008 till July 2010, 98 patients were intubated for mechanical ventilation. Out of them, 69 patients were enrolled in the study. Patients who expired or left against medical advice before 48 hours of ventilation were excluded from the study. Those who were admitted to ICU with diagnosis of pneumonia or had any infiltrations in the chest X-ray at the time of ICU admission were also excluded.

Baseline characteristics which included age, gender, admitting diagnosis, indication for mechanical ventilation, and oxygenation (PaO2/FiO2) prior to onset of VAP were noted. These patients were prospectively followed for development of pneumonia. VAP was diagnosed as per CDC criteria.[7]

Patients who are mechanically ventilated for more than 48 hours, with occurrence of new and persistent infiltration in the chest roentgen, together with any two of the following:

1. Fever, defined as temperature >38°C

2. Leukocytosis, defined as total leukocyte count >10X10^3

3. Purulent tracheal aspirate

Chest X ray was done at the time admission and repeated every day. This diagnosis was confirmed by the presence of organisms on culture of tracheal aspirate. The tracheal aspirates were sent for gram staining and microbial analysis – culture and antibiotic sensitivity done routinely after 48 hours of mechanical ventilation. This was repeated at 48 hours if initially negative. The organisms detected on culture of tracheal aspirate were charted for the purpose of identifying the causative agent. Antibiotics were changed as per sensitivity pattern. Total leukocyte count was done as indicated by the admitting diagnosis or routinely at 48 hours or as indicated by chest X-ray findings.

The patients who developed VAP or met the above criteria within 96 hours of mechanical ventilation were categorized as early onset VAP and those who developed the same after this time period were categorized as late-onset VAP.

All the patients were managed with routine strategies for mechanical ventilation: semi-recombinant position at 45°, sedation and analgesia with midazolam and morphine/ fentanyl titrated to tube tolerance, chlorhexidine oral care, deep vein thrombosis prophylaxis, active and passive chest physiotherapy by the physiotherapist. None of the patients were paralyzed.

The incidence of VAP was noted and each surrogate variable was analyzed. The surrogate variables that included risk factors for VAP were re-intubation, peptic ulcer prophylaxis, enteral feeding, invasive lines, use of ionotrops, low initial PaO_2/FiO_2 ratio and steroid use. Each of these variables were noted and compared between 2 groups – VAP and non-VAP. Although called for, the APACHE score was not done in our study as it was not feasible for all the patients at our center to bear the cost of all the investigations necessary. Investigations were limited to the very essential ones due to cost constraints.

The outcome of the disease was measured by length of ICU stay and duration of mechanical ventilation. The data was entered and tabulated in Microsoft Excel. The statistics were analyzed using website: http://www.graphpad.com. The obtained data were subjected to the univariate analysis using the chi-square test. Comparison of data comprising mean± SD was done with the help of t-test. P-values less than 0.05 were considered as significant. We included the risk factors for chi-square test, and age and duration of mechanical ventilation/ ICU stay for t-test (as it contains data comprising of mean +/- SD).

RESULTS

During the period of study, 98 patients were mechanically ventilated. Out of them, 8 were with initial diagnosis of pneumonia, 6 had left against medical advice and 15 had expired before 48 hours. These patients were excluded from the study. Sixty nine patients were enrolled in the study. Out of them, 28 (40.58%) were male and 41 (59.42%) were female (Table 1). The mean age of the patients was 33.66± 18.84. Among the patients, 22 (31.88%) developed VAP. Mean PaO2/ FiO_2 was 211 for VAP and 286 for non VAP patients.

Table 1. Demographic data of the study patients

	VAP	Non-VAP	Total	p-value
Male	10	18	28	0.57
Female	12	29	41	
Age (mean±SD y)	32.69±23.75	43.33±25.37	-	0.10

The clinical spectrum of the study patients are demonstrated in table 2. The most frequent of the cases were organophosphate poisoning. Other frequent cases were 12 patients post abdominal surgery and 13 patients with septicemia. Higher incidence of VAP occurred in poisoning, post laparotomy and COPD.

Table 2. Clinical spectrum of different disease conditions.

Admission diagnosis	VAP	Non-VAP	Total	Percentage
Poisoning	7	16	23	30.43
Abdominal surgery	4	8	12	33.33
Septicemia	3	10	13	23.07
COPD	4	4	8	50
Neurological (meningitis, encephalitis, GBS, stroke)	1	5	6	-
Trauma	2	2	4	-
Metabolic disorders / dyselectrolytemia	1	3	4	-
Pulmonary embolism	0	1		-
Fat embolism	0	1		-
Pneumothorax	0	2		-

The total number exceeds the actual total due to some patients with multiple diagnosis.

COPD=Chronic Obstructive Pulmonary Disease, GBS=Guillain Barre Syndrome

Patients requiring inotropes or vasopressors, invasive lines had significantly higher incidence of VAP. Use of peptic ulcer prophylaxis, H_2 blockers was also significantly associated with VAP. Development of VAP was similarly high in patients who were initially hypoxic – PaO_2/FiO_2 ratio< 200. Out of 18 patients who required re-intubation, 12 of them developed VAP, which was highly significant (P< 0.001). The incidence of VAP was significantly less in enterally fed patients. Out of 47 enterally fed patients, only 19 developed VAP and this was statistically significant. Use of steroid did not result in significant increase in incidence of VAP in our study cohort.

Table 3. Risk factors associated with VAP

Risk factors	Total	VAP	Non-VAP	p-value
Ionotrops/vaso-pressors	25	13	12	0.006
CVP/arterial lines	41	21	20	0.001
H2 blocker	24	12	12	0.018
PaO_2/FiO_2 <200 on day 2	19	10	9	0.023
Enteral feed	47	19	28	0.026
Steroids	21	7	14	0.86
Re-intubation	18	12	6	<0.001

CVP=central venous pressure, H_2blockers= histamine receptor 2 blocker, PaO_2/FiO_2=arterial partial pressure of oxygen/fraction of oxygen in inspired air.

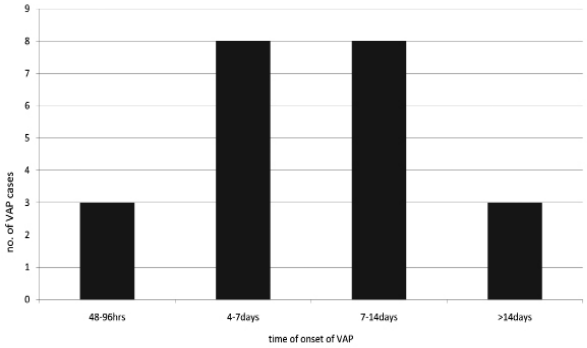

Figure 1. Shows the onset of VAP. Only 3 out of 69 developed early onset VAP. Most of the VAP occurred between 4 days to 2 weeks.

The causative organisms isolated from culture of tracheal aspirate are shown in Table 4. Out of 32 cultures from 22 VAP patients, the most common organism was found to be *Acinetobacter bumanii*. Four culture reports revealed more than one organism. Majority of microbes were gram negative. *Klebsiella sp*. was commonly found in early-onset pneumonia. No cases had methicillin resistant *Staphylococcus aureus*.

Table 4. Causative organisms of VAP

Organism	Early onset	Late onset
Staphylococcus aureus (MSSA)	2	-
Klebsiella sp.	5	4
Pseudomonas aeroginosa	-	6
Acenobacter baumanii	-	11
E.coli	-	5
Enterococcus sp	-	4

Out of 22 patients who developed VAP, 13 (59.1%) required tracheostomy indicated for prolonged need of mechanical ventilation (Table 5). The duration of mechanical ventilation for the VAP group was significantly high (p<0.001). Similarly, the VAP group also had significantly longer duration of ICU stay (p=0.006). Crude mortality in the study cohort was 21.9%. The mortality rate for VAP group was 22.2% and for non-VAP was 21.74% with no significant difference between the two.

Table 5. Outcome of mechanically ventilated patients

Outcome	Total	VAP	Non-VAP	p-value
Tracheostomy	13	10	3	<0.001
Duration of MV(mean±SD d)	-	18.88±7.7	7.36±4.19	<0.001
Duration of ICU stay (mean±SD d)	-	29±17.88	9.22±5.14	0.006

MV=mechanical ventilation

DISCUSSION

VAP stands as a co ts were found to be age >70, re-intubation, intraoperative inotropic support, transfusion, days of mechanical ventilation, emergent surgery.[12] Use of steroids, however, did not seem to be a risk factor for development of VAP in the present study, though some studies identified this as a risk factor.[12]

Though enteral feed via nasogastric tube has been stated as a risk factor due to increased gastric pH, volume and regurgitation, it may have improved the nutritional status, decreased gut translocation and prevented VAP in our patients. [14,15] Intermittent feed, semi- recombinant position at 45°, avoidance of gastric over distension and use of pro-kinetics when required, has decreased the incidence of VAP in some studies.[16,17] Similar finding was observed in our study.

Tracheostomy has also been stated as a risk factor by some studies.[8,10] However, some studies state that early and planned tracheostomy protects mechanically ventilated patients from VAP.[9] Our patients rather had late tracheostomies between 7-14 days. So this was studied as an outcome of VAP and need of prolonged mechanical ventilation.

Although morbidity and ICU stay was prolonged in our patients with VAP, the mortality was similar for both groups. Other studies[18] also reported similar outcomes.

Gram negative bacteria, *Pseudomonas aeruginosa* and *Acinetobacter baumanii* are commonly associated with late onset VAP.[19, 20] Our ICU patients had *Acinetobacter sp*. as the most common causative microbe.

In our study, we used a qualitative study of tracheal aspirate (TA) rather than quantitative bronchioalveolar lavage (BAL) because of its ease, cost effectiveness and equivalence in sensitivity.[21,22] A study by Daren Heyland had concluded that similar outcomes and use of antibiotics result whether the diagnosis of VAP is made by TA or BAL.[21]

CONCLUSION

The incidence of ventilator-associated pneumonia is high in our setting. Gram negative bacteria causing late-onset VAP is common. Patients who require invasive lines, inotropes, re-intubation, H_2 blockers, are at high risk. Requirement of mechanical ventilation for more than four days increases the risk. These patients need special attention towards preventive measures such as hygiene, proper weaning protocol, early and planned tracheostomy.

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