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Original Article

Incidence and Risk Factors Association for Ventilator Associated Pneumonia in Neontal Intensive Care Unit

Naresh Kumar, Preeti Malhotra, Amanjeet Kaur Bagga, Gagandeep Kaur

Department of Paediatrics, Sri Guru Ram Das Institute of Medical Sciences and Research, Mehta Road, Post Office Vallah, Amritsar, Punjab – 143501, India.

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***Corresponding Author**

Preeti Malhotra
Professor,
Department of Paediatrics,
Sri Guru Ram Das Institute of Medical Sciences and Research,
Mehta Road,Post Office Vallah,
Amritsar, Punjab – 143501, India
Email: gagan2904@hotmail.com

Abstract

Introduction: Ventilator Associated Pneumonia (VAP), the nosocomial pneumonia developing in mechanically ventilated patients after 48 hours of mechanical ventilation, is the second commonest nosocomial infection in the neonatal intensive care unit (NICU). VAP occurring within 96 hours of initiation of mechanical ventilation is termed as early VAP and later than that is known as late VAP. The aim of this study was to determine the incidence rate and risk factors of early and late ventilator associated pneumonia in NICU.

Methods: The study was conducted from December 2015 to November 2017 in which 40 neonates were ventilated for more than 48 hours of which those who developed VAP as per CDC criteria were enrolled in the study. Birth weight, gestation age, reintubation if needed and number of days of ventilation were noted. Statistical associations were further evaluated between various parameters of VAP and time of development of VAP.

Results: Incidence of Early VAP was 12.5% and that of Late VAP was 87.5%. 93.95% neonates who were reintubated developed VAP. Duration of mechanical ventilation and re-intubation were significantly associated with the time of development of VAP. Birth weight and gestation age were statistically insignificant factors in determining VAP.

Conclusions: Re-intubation and duration of mechanical ventilation are a significant risk factor for development of late VAP. Gestation age and birth weight have been identified as additional risk factors. Early diagnosis is necessary for appropriate treatment and decreased hospital stay.

Introduction

Ventilator associated pneumonia (VAP) in Neonatal Intensive Care Unit (NICU) is defined as pneumonia in mechanically ventilated neonates, that develops at 48 hours or later after the neonate has been put on ventilator. VAP is the second most common nosocomial infection among neonatal intensive care unit patients.[1,2] VAP occurring within first four days of initiation of mechanical ventilation (< 96 hours) is termed as early onset pneumonia while pneumonia occurring after four or more days(> 96 hours) is known as late onset pneumonia.[3]

In neonates, most common cause of assisted ventilation is respiratory failure which occurs in the form of apnoea or compromise in pulmonary gas exchange (Primary lung

disease). Repeated episodes of prolonged apnoea unresponsive to other measures viz.caffeine citrate, physical stimulation and associated with bradycardia or cyanosis, should be treated with CPAP or assisted ventilation. In the cases of primary lung disease, physiological alterations in gas exchange cause acidosis, hypercapnia and hypoxia which are indications for ventilation.[4]

Looking onto the neonatal population, the incidence of VAP is highly influenced by gestational age and regional financial development. Hence, while in developed countries the incidence of VAP in neonates is between 2.7 to 10.9 episodes per 1000 ventilator days while in developing countries itreaches upto 37.2 cases per 1000 ventilator days.[5-8] Statistical studies in NICU patients indicate that pneumonia comprises 6.8% to 32.3% of nosocomial infections.[9] According to data published by the National Nosocomial Infection Surveillance System (NNIS) program sponsored by the Centre for Disease Control and Prevention (CDC), VAP rates in NICU account upto 30% of nosocomial infections and complicates the hospital course of eight to 28% cases.[10]

VAP is due to invasion of lower respiratory tract and lung parenchyma by microorganisms which is mainly because of disruption of integrity of oropharynx and trachea.[5] Pathogens can reach the lung from sources like hands of healthcare workers, ventilator circuits and biofilm of endotracheal tubes.[11] Interventions for VAP prevention include hand hygiene, bed elevation to 30- 45 degrees, oral care with chlorhexidine, use of orogastric tubes and use of closed system suctioning.[12,13] To reduce the burden of VAP in NICU and PICU, it is important to follow guidelines to prevent its development using bundle approach.[14-17]

Methods

The present study was conducted in the Department of Paediatrics in collaboration with the Department of Microbiology, of Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, India. Forty neonates who developed VAP as per CDC criteria were enrolled as subjects. It was a prospective observational study in which 40 neonates, diagnosed as VAP as per CDC guidelines, were taken as subjects after approval from Institution Thesis and Ethical Committee and after taking informed consent from parents.Neonates who required mechanical ventilation for aperiod of 48 hours and developed VAP as per CDC criteria, in NICU were enrolled. Babies with congenital cardiac condition requiring mechanical ventilation or neonates mechanically ventilated for less than 48 hours and transferred from other hospital were excluded from the study. VAP was considered in those with mechanical ventilation for > 48 hours and fulfilling CDC criteria. Neonates were ventilated using standard NICU protocol. Ventilation was done by endotracheal tube with heated humidification system. One set of disposable ventilation circuit was used per neonate. Open method of suction was done for suctioning secretions.Clinically, patients must have at least three of the following criteria:

- Fever (> 38.4°C or > 101.1°F) or hypothermia (< 37°C or 97.7°F) with no other recognized cause;
- Leukopenia (< 4,000 mm^3) or leucocytosis (15,000 mm^3);
- Worsening respiratory distress, increased respiratory secretions, or increased suctioning requirements;
- Rales or bronchial breath sounds;
- Worsening gas exchange {O_2 desaturations (pulse oximetry of < 94%), increased oxygen requirements, or increased ventilation demand}

Baseline TLC, DLC and chest Xray AP view were done in all patients at the time of initiation of ventilation. Blood culture was sent on the day of admission. Subsequent blood count estimation and blood cultures were sent on the day on which pneumonia was suspected by the onset of new clinical signs as per CDC. The data of VAP patients was tabulated into various categorical variables which were presented in number and percentage (%) and continuous variables as mean +- SD. Qualitative variables were correlated using Chi Square test / Fischer's exact test. A p value of < 0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Results

Table 1. Demographic variables

		Percentage(n)
Inborn / Outborn	Inborn	42.5 (17)
	Outborn	57.5 (23)
Sex	Male	82.5 (33)
	Female	17.5 (7)
Mode of delivery	NVD	62.5 (25)
	LSCS	37.5 (15)
Indication of ventilation (Clinical diagnosis)	Respiratory Distress Syndrome	35 (14)
	Perinatal asphyxia	35 (14)
	Septicaemia	22.5 (9)
	Congenital pneumonia	7.5 (3)
Reintubation	Yes	82.5 (33)
	No	17.5 (7)
Time of development of VAP	< 96hours (early VAP)	12.5 (5)
	> 96 hours (late VAP)	87.5 (35)
Total leukocyte count	Leukocytosis	47.5 (19)
	Leukopenia	45 (18)
Radiological findings	Consolidation	55 (22)
	Infiltrates	42.5 (17)
	Pneumatocele	2.5 (1)

Forty neonates who were intubated for more than 48 hours in the NICU and developed VAP as per CDC guidelines, were studied till death or discharge and the following observations were made. It was observed that 57.5% were inborn and 42.5% were outborn neonates and overall male preponderance was seen with ratio being 82.5:17.5. Most common indication of ventilation in the

study group was respiratory distress as seen in 52.5% followed by perinatal asphyxia in 27.5%, apnea in 10% and seizures in 10%. 82.5% neonates required reintubation and 12.5% neonates developed VAP before 96 hours of initiation of mechanical ventilation whereas 87.5% developed VAP after 96 hours of initiation of mechanical ventilation. VAP was radiologically confirmed as consolidation in 55% cases, formation of new infiltrates in 42.50% and pneumatocele in 2.5%.

Out of the total 40 cases, eight were born between 26 to 28 weeks gestation and all of them developed late VAP. Nine were born between 29 to 32 weeks gestation and all of them developed late VAP. Fifteen were born between 33 to 37 weeks gestation, out of which 20% developed early VAP and 80% late VAP. Eight cases were born after 37 weeks of gestation, out of which 25% developed early VAP and 75% late. (P =0.326)

It was seen that out of 40 neonates, four were ELBW and all of them developed late VAP. Fifteen were VLBW out of which 6.67% developed early VAP and 93.3% late VAP. Five had birth weight between 1.5 to two kg, out of which 20% developed early VAP and 80% late VAP. Ten neonates had birth weight between two to 2.5kg, out of which 10% developed early VAP and 90% late VAP. Six neonates had birth weight of > 2.5kg, out of which 33.33% developed early VAP and 66.67% late VAP (P = 0.601)

Among 40 neonates, 33 were reintubated, out of which 6.06% developed early VAP and 93.94% developed late VAP. Seven neonates were not reintubated and out of 42.86% developed early VAP and 57.14% developed late VAP(P = 0.030).

Out of total 40 neonates who developed VAP, two neonates were ventilated for two to four days and 100% of them developed early VAP. Twelve neonates were ventilated for four to seven days out of which 8.33% developed early VAP and 91.67% developed late VAP. Twelve neonates were intubated for seven to ten days out of which 16.67% developed early VAP and 83.3% developed late VAP. Majority of the neonates i.e. 14 were intubated for more than 10 days and 100% of them developed late VAP (P =0.001).

Table 2. Association of time of VAP development with various variables

		Early VAP	Late VAP	P value
Gestation age (Weeks)	26-28	0% (0)	100% (8)	0.326
	29-32	0% (0)	100% (9)	
	33-37	20% (3)	80% (12)	
	>37	25% (2)	75% (6)	
Birth weight (kg)	<1	0% (0)	100% (4)	0.601
	1-1.5	6.67% (1)	93.3% (14)	
	1.6-2	20% (1)	80%(4)	
	2.1-2.5	10% (1)	90% (9)	
	>2.5	33.33% (2)	66.67% (4)	
Reintubation	Yes	6.06% (2)	93.94% (31)	0.030
	No	42.8% (3)	57.14% (4)	
Days of mechanical ventilation	2-4	100% (2)	0% (0)	0.001
	4-7	8.33% (1)	91.67% (11)	
	7-10	16.67% (2)	83.33% (10)	
	>10	0% (0)	100% (14)	

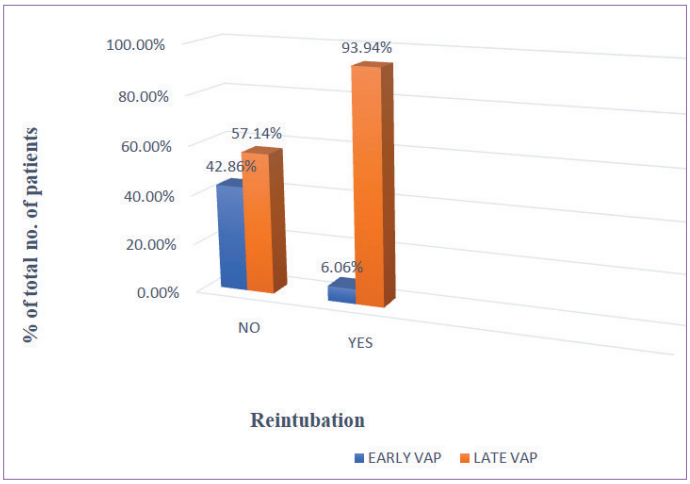

Figure 1. Reintubation and early and late VAP

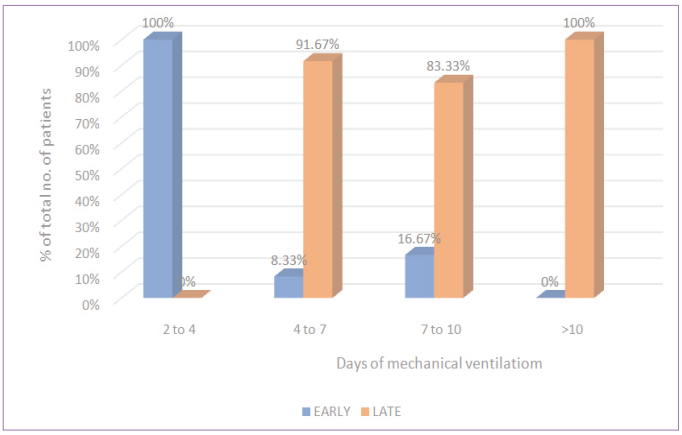

Figure 2. Days of mechanical ventilation with early or late VAP

Discussion

During the study period, 550 neonates were admitted in NICU, out of which 216 were ventilated for more than 48 hours. Incidence of VAP in neonates was 18.5%. This incidence was comparable to the study of Yuan TM et al being 20.1% whereas Tripathi S et al, Apisaranathak et al have shown the incidence of 30.6% and 28.3% respectively.[7,18] In our study, males accounted for 82.5% of neonatal cases which is primarily because of male preference in developing country like ours. Similar results were found in the study done by Lee PL et al on neonates, where VAP was reported in 66.7% males[19]and Khattab A et al also reported a 70.2% male preponderance in neonates.[20]

Majority of neonates in the study were premature, accounting for 32 cases out of total 40 (85%) and only two were post term (5%) with mean gestation age of 33.2+- 4.49 weeks. But gestational age of neonates had no statistical significance to the development of early or late VAP. In the study done by Badr MA et al, mean gestational age of neonates who developed VAP was 33.6+- 3.2 weeks and was a significant risk factor for development of VAP (P = 0.04). This was comparable to our study.[21] Foglia et al and Chastre J et al also reported that incidence of VAP increases with decreasing gestation age.[10,22]

Birth weight is a significant risk factor for development of VAP. In our study, amongst 40 neonates who developed VAP, 34 (85%) were LBW and out of these, 15 were VLBW. LBW had no statistical significance to development of early or late VAP (P =0.601). In a cross sectional study, Stover et al reported higher incidence of VAP in VLBW neonates.[23] In another study done by Deng C et al, LBW was present in 67.5% neonates and was significantly associated with development of VAP.[24]

In our study, 82.5% neonates were reintubated and the incidence of more than two times was seen in 36% neonates. Sixty percent neonates were reintubated in the study done by Tripathi S et al which proved to be statistically significant for the development of VAP (p< 0.001).[7] According to Yuan TM et al, risk factors of neonatal VAP were reintubation, duration of mechanical ventilation, treatment with opiates and endotracheal suctioning.[25]

We found that reintubation was significantly associated with duration of mechanical ventilation (P = 0.002) and development of late VAP (P = 0.030). Studies on reintubation and its association have been conducted on adult population but not on pediatrics population. Our study reveals that 35% neonates were ventilated for more than 10 days. Prolonged duration of ventilation increases the risk of infection. Duration of mechanical ventilation is reported to be one of the most common neonatal risk factors leading to the occurrence of VAP by Elward AM et al,[26] Foglia E [10] and Yuan TM et al.[25] According to the study conducted by Tripathi S et al, the duration of mechanical ventilation is an independent and significant risk factor for predicting VAP. The mean duration reported was 300.2+-174.6 hours.[7]

The most common cause of admission in NICU was respiratory distress. Most common clinical diagnosis leading to ventilation was hyaline membrane disease and perinatal asphyxia (35% each). Deng C et al reported lung disease, especially neonatal RDS as the most common presenting complaint in VAP patients. [24]Badr MA et al also found respiratory distress syndrome in 35.9% neonates who developed VAP.[21] In the study by Azab SF et al, primary cause of ventilation was prematurity and related complications (74%) followed by perinatal asphyxia (9.7%).[27] In this study, VAP was confirmed radiologically by the presence of consolidation in 55% neonates and new, progressive or persistent infiltrates in 42.5%. Khattab A et al reported progression of infiltrates in 72.3% cases which was statistically significant for VAP.[20] Srinivasan et al reported that presence of new radiological changes is associated with VAP in children.[28]

Conclusions

Reintubation and duration of ventilation were seen as prominent factors causing VAP, especially late VAP. LBW and prematurity were additional risk factors for development of late VAP in neonates. This necessitates identifying them timely, accurate diagnosis and timely initiation of antibiotic therapy.

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