Original article:

Ventilator-associated Pneumonia in a Paediatric Intensive Care Unit – a Prospective Cohort Study

Dr Pramila Borse [1] Dr Jane J.E. David[2]

Senior Resident of Pediatrics[1]

Assistant Professor of Pediatrics[2]

Department of Pediatrics T.N.Medical College & B.Y.L Charitable Hospital,Mumbai Central,Mumbai,India

Correspondence: Dr Jane J.E.David,Department of Pediatrics,Seth G.S.Medical College & KEM Hospital,Parel ,Mumbai -400012

Abstract

Introduction: Ventilator-associated pneumonia(VAP) is the second most common nosocomial infection in the Paediatric Intensive Care Unit (PICU) and is estimated to occur in 3-10 % of ventilated patients. Objectives: To study the incidence, aetiology, risk factors and outcome of VAP in the PICU. Methods: All consecutive patients who were ventilated for more than 48 hours were prospectively enrolled. Patients with pre-existing pneumonia were excluded. VAP was diagnosed using the modified Clinical Pulmonary Infection Score (CPIS). Portable chest X-ray and culture of tracheal secretions was done in all patients suspected of having VAP (CPIS >6). Risk factors for VAP were identified by univariate and multivariate analysis using appropriate statistical methods. Results: The mean age of the study population was 53+45 months. Male to female ratio was 1.3:1.Thirty-one of 70 (44.3%) patients developed VAP. Organisms were isolated from 8 of 31 patients with VAP, Pseudomonas aeruginosa being the most common pathogen.Repeated intubation, presence of central venous lines and duration of ventilation and PICU stay were found to be significantly associated with VAP on univariate analysis. On multivariate analysis, only duration of ventilation was found to be significant risk factor for VAP. Mortality in patients with VAP was 55.6% as compared with 38.5% in those without VAP. Conclusion: The frequency of VAP in our study was 44.3%. Gram-negative organisms were the most common pathogens isolated from tracheal secretions. Duration of ventilation was a significant risk factor for VAP. Mortality in patients with VAP was 55.6%.

Key Words: Pneumonia, Ventilator-Associated; Intensive Care Units, Pediatric; Healthcare Associated Infections

Introduction

Ventilator-associated pneumonia (VAP) is defined as pneumonia which occurs 48 hours or later after the initiation of mechanical ventilation in patients who did not have pneumonia at the time of intervention[1]. Health care-associated infections have been reported to occur in approximately 12% of patients admitted to the paediatric intensive care unit (PICU) with VAP being the second most common type of hospital-acquired infection[2]. VAP has been estimated to occur in 3-10% of ventilated patients in the PICU [3,4]. Though VAP has been extensively studied in adults, studies in children, especially from India, are limited. This study was therefore done, to determine the frequency, aetiology, risk factors and outcome of VAP in children admitted to a PICU in a tertiary care public hospital.

Patients and methods

This was a prospective cohort study conducted in the paediatric intensive care unit (PICU) of the T.N.Medical College &B.Y.L.Nair Charitable

Hospital, a tertiary care public hospital in Mumbai. The PICU has 6 beds and caters to patientsbetween 1 month and 12 years of age, admitted with medical conditions. The PICU has between 300-400 admissions per year. Neonates, paediatric surgical and trauma patients are admitted elsewhere in the hospital.

All consecutive children admitted to the PICU over a 1-year period between November 2014 and October 2015 and requiring mechanical ventilation for 48 hours or more were included in the study. Children with pre-existing pneumonia were excluded.

All patients ventilated for 48 hours or more were followed up for development of ventilator-associated pneumonia. Ventilator–associated pneumonia (VAP) was defined as that occurring 48 hours or longer after initiation of mechanical ventilation via tracheostomy or endotracheal tube and was diagnosed using the modified Clinical Pulmonary Infection Score (CPIS)[5]. The score is based on six variables: temperature, blood leukocyte count, volume and purulence of tracheal secretions, oxygenation, pulmonary radiography, and semi-quantative culture of tracheal aspirate. Scores can range between zero and 12 with a score of 6 or more showing good correlation with the presence of VAP.

The following details were recorded on the case record form: demographic data, clinical features, primary diagnosis, laboratory and radiographic investigations, treatment including antibiotics, course in the PICU, duration of ventilation, duration of PICU stay and outcome in terms of discharge or death.Portable X-ray of the chest, blood culture and culture of endotracheal secretions were done in patients suspected to have VAP. Endotracheal secretions were collected under aseptic conditions, by gentle aspiration, using an 8F suction catheter. The sample was transported in a sterile container to the laboratory where it was plated for microbiological culture. Antibiotic sensitivity pattern was obtained in patients with a positive culture. All patients were followed up until discharge from the PICU or death.

Patients were enrolled after informed consent from the parent or guardian. The study was approved by the Institutional Ethics Committee.

The data of patients who developed VAP was compared with patients who did not develop VAP to identify risk factors for the development of VAP. Categorical variables were compared using Pearson Chi-square test and Fisher'sExact tests and continuous variableswith the nonparametric Mann-Whitney test.A p value of less than 0.05 was considered significant. Variables found to be significantly associated with VAP were subjected to stepwise logistic regression analysis. SPSS version 16.0 was used for analysis.

Results

During the study period, a total of 102 of 368 admissions to the PICU were ventilated for 48 hours or more. In thirty-two of them, the indication for ventilation was pneumonia and hence these were excluded from the study. A total of 70 patients fulfilled the inclusion criteria and were enrolled.

The mean age of the study population was 53 + 45 months with a male to female ratio of 1.3:1. Demographic features, underlying illness, procedures done, organisms grown and outcome are summarised in table 1.

Thirty-one of the seventy study patients (44.3%) developed ventilator-associated pneumonia. Gram negative organisms were isolated from the tracheal aspirates in seven of thirty-one patients with VAP, with Pseudomonas aeruginosa being the predominant organism.

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The probable risk factors like demographic characteristics, underlying illness, procedures performed and duration of ventilation and PICU stay, were compared in patients who developed VAP with those who didnot develop VAP. The results are summarised in table 2.There was no statistical difference between the two groups with respect to age, gender or underlying illness. Mortality in patients who developed VAP was 55.6% as compared with 38.5% in those who did not develop VAP; however this was not statistically significant. Reintubation, presence of central venous lines and duration of ventilation and PICU stay were found to be significant risk factors on univariate analysis. These factors were further subjected to logistic regression analysis (table 3). Only duration of ventilation was found to be an independent risk factor for the development of VAP.

Discussion

We used the modified Clinical Pulmonary Infection Score (CPIS) for the diagnosis of VAP. Clinical criteria for VAP include fever, leucocytosis or leucopoenia, and presence of tracheal secretions which by themselves are non-specific and have poor sensitivity and specificity for the underlying pathology. Also,a positive trachealculture alone does not discriminate between bacterialcolonization and respiratory infection. Hence, these criteria must be combined with radiological and microbiological criteria. In a study of 70 children with VAP, da Silva and co-workers found a modified clinical pulmonary infection score (mCPIS) of six or higher to have a sensitivity of 94%, a specificity of 50%, a positive predictive value of 64%, a negative predictive value of 90%, and positive and likelihood ratios of 1.9 and 0.1, respectively[7].

The frequency of ventilator associated pneumonia in different regions of the world is summarised in table 4.The range of VAP incidence is very large, with higher rates observed in the lower-middle-income countries [4,8,10,11,13,14] as compared with the upper-middle-income countries [3,15,16].Extremely high rates have been reported from India (36.2%) [8]. Our study showed a VAP frequency of 44.3%.

Various risk factors for VAP have been reported.We found no significant association of VAP with intrinsic factors such as age or gender.Extrinsic risk factors reported in literature include reintubation, prior antibiotic therapy, bronchoscopy, immunosuppressive therapy and use of enteral feeding. [18,19] In our study, reintubation, the presence of central venous lines and duration of ventilation and PICU stay were found to be significantly associated with VAP on univariate analysis. However on logistic regression analysis only the duration of ventilation was found to be significantly associated with VAP. This was also reported by Awasthi and co-workers from Lucknow[8].

Gram negative organisms were the predominant isolates from tracheal aspirates in our patients, with Pseudomonas aeruginosa being the most common followed by Klebsiella pneumoniae and Acinetobacter species. No organisms were grown from the tracheal aspirates of patients who did not develop VAP. Organisms isolated and the antibiotic susceptibilities vary according to geographical region. Isolation of Gram-negative organisms is highest in Asia with the most common pathogens being Pseudomonas aeruginosa, Acinetobacter baumannii and enterobacteriaceae[20,21,22]. Additionally, most pathogens in Asia are multidrug resistant[22]. In contrast, in Europe and North America, Staphylococcus aureus is the most common pathogen isolated [19,23].

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Many interventions have been shown to play a role in the prevention of VAP. These include hand hygiene preferably with alcohol-based hand rub, use of gown and gloves for endotracheal tube adjustment,elevation of backrest to 30°-45°, oral care with chlorhexidine,prophylaxis for stress ulcers,maintenance of endotracheal cuff pressure, use of orogastric rather than nasogastric tubes, avoidance of gastric overdistension andelimination of nonessential tracheal suction [24].

The VAP rate in our PICU was 44.3% . This has prompted initiation of an education program targeting resident doctors and nurses posted in the PICU. The program includes training in handling of ventilator circuits, oral suctioning, hand hygiene, oral care with chlorhexidine and elevation of backrest. Visitors to the PICU have also been restricted. The INICC multidimensional infection control program was implemented in the NICUs from 10 developing countries and was associated with significant reductions of VAP rates at baseline and intervention were 17.8/1000 and 12.0/1000 ventilator-days, respectively [25].

The mortality in patients with VAP was 55.6% as compared with 38.5% in patients without VAP.High mortality rates have also been reported from other countries in Asia [9,10] underlining the urgency for adoption of preventive strategies.

In conclusion, VAP was seen in 44.3% of children in our study. Gram-negative organisms were the predominant isolates from tracheal secretions. There was a significant association between development of VAP and duration of ventilation. Mortality in children who developed VAP was 55.6%.

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Table 1. Profile of study patients

Patient characteristics	**Number (Total=70)**
Demographic data	
Age in months (mean+S.D.)	53 + 45
Sex Males Females	39 31
Underlying condition	
Central nervous system	33
Neuromuscular	6
Gastro-intestinal/hepatic	6
Heart disease	5
Renal	2
Hematological	1
Others	17
Procedures done	
Central venous line	49
Reintubation	42
Ventricular shunt	7
Tracheostomy	3
Dialysis	1
Organisms grown in tracheal aspirate (n=7)	
Pseudomonas aeruginosa	3
Klebsiella pneumoniae	2

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Acinetobacter species	2
Outcome	
VAP	31 (44.3%)
Duration of ventilation (days) Mean + S.D.	6.55 + 5.24
Duration of PICU stay (days) Mean + S.D.	9.82 + 8.16
Death	31

Table 2. Frequency and univariate analysis of variables in patients with and without VAP

Variable	**Number of patients (n=70)**		**P value**
	With VAP (n=31)	**Without VAP (n=39)**	
Mean age in months	54.52+41.37	55.92+37.54	0.72786[a]
Male sex	19	21	0.62920[a]
Primary diagnosis			
Central nervous system disorder	16	17	0.50416[b]
Neuromuscular	4	2	0.39499[c]
Gastro-intestinal/hepatic	1	5	0.217166[c]
Cardiovascular	2	3	1.000000[c]
Renal	1	1	1.000000[c]
Hematological	0	1	1.000000[c]
Others	7	10	0.76677[b]
Procedures			
Reintubation	26	16	0.000278[b]
Central venous line	26	23	0.023955[b]
Ventricular shunt	3	4	1.00000[c]
Tracheostomy	3	0	0.082115[c]
Dialysis	0	2	0.499379[c]
Duration of ventilation	9.45+4.78	4.46+1.08	0.00000[a]
Duration of PICU stay	13.03+7.85	7.26+2.85	0.00244[a]
Mortality	16 (55.6%)	15 (38.5%)	0.08000[a]

[a] Non-parametric Mann Whitney test

[b]Chi-square test

[c] Fischer's exact test

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Table 3. Logistic regression analysis of risk factors associated with the development of VAP

Variable	**p value**	**Odds ratio(95% CI)**
Reintubation	0.2536	2.2556 (0.5582-9.1150)
Presence of central venous lines	0.2083	2.5664 (0.5912-11.1404)
Duration of ventilation	0.0025	2.4834 (1.3759-4.4825)
Duration of PICU stay	0.6010	0.8331 (0.6888-1.0078)

Table 4: Frequency of ventilator associated pneumonia in the PICU in different geographic regions

Region	**Reference (author, country, year of publication and reference no.)**	**No. of patients**	**VAP**	**%**
South-east Asia	Awasthi, India,2013 [8]	105	38	36.2
	Balasubramaniam, India, 2014,[9]	232	14	6.03
	Hamid, Pakistan, 2012 [10]	93	16	17.0
	Sharma, Maldives, 2009 [11]	40	8	20.0
Middle East	Almuneef, Saudi Arabia, 2004 [4]	361	37	10.3
East Asia	Navoa-Ng, Philippines, 2011 [12]	252	6	2.4
Africa	El-Kholy, Egypt, 2012 [13]	211	54	25.6
South America	Casado, Brazil, 2011 [14]	366	39	10.7
Europe	Patria, Italy, 2013 [15]	451	30	6.7
	Jordan Garcia, 2014, Spain [16]	300	4	1.3
North America	Elward, USA, 2002 [3]	595	34	5.1
Australia	Gautam, Australia, 2012 [17]	269	18	6.7

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