Research Article

Risk factors, pathogen profile and outcome of ventilator associated pneumonia in a Neonatal intensive care unit

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Received: 12 December 2014
Accepted: 23 January 2015

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Abstract

Background: Objective of current study was to know the risk factors, pathological profile and outcome of ventilator associated pneumonia in the neonatal intensive care unit.

Methods: Design: Prospective observational study. Settings: A teaching, referral, neonatal intensive care unit at Srinagar, Kashmir. Participants: All ventilated neonates who required mechanical ventilation for more than 48 hours between August 2011 to July 2012. Procedure: The diagnosis of VAP was made on the basis of criteria given by National Nosocomial Infection Surveillance System (1996), paediatric modification of the original guidelines given by Centre of Disease Control & prevention (CDC). Risk factors for VAP were assessed by bivariate and multivariate analysis. Semi-quantitative culture was done using blood agar, chocolate agar and McConkey’s agar as plating media.

Results: VAP developed in 32 of 96 ventilated neonates (33.34% VAP rate). Prematurity, very low birth weight, use of nasogastric tube, mean duration of mechanical ventilation, NICU stay in days and number of endotracheal tube changes were statistically significant risk factors associated with VAP. Multiple logistic regression analysis revealed that duration of mechanical ventilation (P = 0.006) and VLBW (<15000 grams) (P = 0.032) were only two single independent and statistically significant risk factors. Most common bacteria isolated from ETA was Klebsiella (37.5%). There were 9 (28.1%) mortalities in VAP group and 14 (21.8%) in non-VAP group, which was statistically insignificant.

Conclusions: A number of measures is required to decrease the incidence of VAP based on the prevalent modifiable risk factors and etiological organisms in NICU. Daily assessments of readiness to wean and use of weaning protocols must be adhered to in NICUs.

Keywords: VAP, BAL, ETA, CDC

Introduction

Ventilator-Associated Pneumonia (VAP) is defined as nosocomial pneumonia in mechanically ventilated patients that develop more than 48 hours after initiation of Mechanical Ventilation (MV).\(^1\) In addition to its high mortality rate compared to other nosocomial infections, VAP is associated with prolonged hospitalisation and considerable medical costs.

Intubation associated lesions of pharynx and trachea lead to bacterial colonization by decreasing ciliary function and swallowing reflex. It inhibits cough reflex and bypasses the body’s humidified airways. Colonisation of upper respiratory tract occurs rapidly and 90% of infants have positive pharyngeal culture by 3rd day.\(^2\) However, bacterial colonisation does not always result in disease. Factors influencing which of the colonized infant will develop disease include prematurity, underlying illness,
invasive procedures, inoculum size, virulence of infecting organism, the innate immune system, host response, and trans-placental maternal antibodies.

The organisms commonly implicated for VAP are gram positive and gram negative bacteria\(^3\) of which Klebsiella is most common culprit.\(^4\) Early onset VAP (within 5 days of ventilation) results from aspiration of endogenous community acquired organisms e.g. S. pneumoniae, H. influenzae, and aerobic gram negative bacilli. Late onset VAP (5 or more days after initiation of ventilation) results from aspiration of gastric/oropharyngeal secretions and is caused by potentially drug resistant organisms like methicillin resistant Staphylococcus and Pseudomonas.

Within the particular context of developing countries, access to knowledge regarding VAP is scant, and there is an insufficient recognition of the importance of surveillance. This study was conducted to know the risk factors, pathological profile and outcome of ventilator associated pneumonia in authors’ neonatal intensive care unit. Such a study is essential to determine the effective strategies for its prevention and formulating an antibiotic policy.

**METHODS**

The study was conducted at post-graduate department of paediatrics, GB Pant Hospital a teaching, referral hospital at Srinagar. It was a hospital based prospective observational study for one year, conducted between August 2011 to July 2012. The study group comprised of all ventilated neonates less than 30 days, admitted in neonatal intensive care unit during the study period who required mechanical ventilation for more than 48 hours. Excluded from the study were:

1. Those with overt symptoms & signs of sepsis or pneumonia at the time of initiation of mechanical ventilation.
2. Those with gross congenital anomalies.
3. Extremely low birth weight babies (<1000 grams).

All the neonates fulfilling the inclusion criteria for the study underwent detailed relevant history and clinical examination which was recorded in a preset proforma. All neonates were ventilated by oro-tracheal tubes of appropriate size which was changed if blocked or displaced. Neonates were ventilated using Maquet-mini servo-i ventilator with heated humidification system. Midazolam was used for sedation. One set of disposable ventilation circuit was used in one patient. Open suction was used. Patients were ventilated in supine position with frequent changing to right/left lateral position and nasogastric tube was used for decompression or feeding. None of the patients received parenteral nutrition or chest tube drainage. We did not use umbilical artery catheterization during the study period. The diagnosis of VAP was made on the basis of criteria given by National Nosocomial Infection Surveillance System (1996), paediatric modification of the original guidelines given by Centre Of Disease Control& prevention (CDC).\(^5\)

1. Radiology: Two or more serial chest radiographs with at least one of the following:
   I. New or progressive and persistent infiltrate.
   II. Consolidation.
   III. Cavitations.
   IV. Pneumatoceles in infants < 1 year.

2. Signs/symptoms/laboratory: Worsening gas exchange (e.g., \(\text{O}_2\) desaturation, increased oxygen requirement, or increased ventilator demand).

And at least three of the following:

1. Temperature instability with no other recognised cause.
2. Leukopenia (<4000 WBC/mm\(^3\)) or Leucocytosis (>15000 WBC/mm\(^3\)) and left shift (>10% band forms).
3. New onset of purulent secretions or change in character of secretions, or increased respiratory secretions or increased suctioning requirements.
4. Apnoea, tachypnoea, nasal flaring with retraction of chest wall and grunting.
5. Wheezing, rales, or rhochi.
7. Bradycardia (<100 beats/minute) or Tachycardia (>170 beats/minute).

Baseline CBC and chest radiographs were done in all patients at the time of initiation of mechanical ventilation. Subsequent blood counts were done on day on which pneumonia was suspected. After baseline chest radiograph, it was repeated after 48 hours of mechanical ventilation, on suspicion of pneumonia and 48 hours after pneumonia was detected to check for persistence of infiltrates. Follow up included clinical examination for pneumonia and chest radiographs after one week of extubation.

For collection of endotracheal aspirate, endotracheal secretions were collected under all aseptic precautions by instilling 1-2 ml of sterile normal saline into the endotracheal tube and then collecting it back with the...
help of polyethylene tubes with a suctioning pressure of 60 mmHg for 8 seconds. The specimen collected was immediately transported to the laboratory within two hours. Semi-quantitative culture was done using blood agar, chocolate agar and McConkey’s agar as plating media. Blood cultures were collected simultaneously whenever there was a suspicion of VAP.

The study was approved by ethics committee.

Statistical analysis

Data was analyzed using SPSS and Graph Pad In-Stat software. Bivariate analysis was done by Chi square and Welch’s corrected t-test. Multivariate analysis was done by multiple regression analysis.

RESULTS

VAP developed in 32 of 96 ventilated neonates who qualified the study (33.34% VAP rate), incidence of VAP was 68.96 cases per 1000 days of mechanical ventilation. Sex, birth asphyxia, age at time of initiation of ventilation were statistically insignificant risk factors for development of VAP. Using Chi square test, prematurity (OR 4.61; 95% CI 1.67-12.72; P = 0.002), very low birth weight (OR 14.54; 95% CI 1.67-126.86; P = 0.005), use of nasogastric tube (OR 3.18; 95% CI 1.31-7.69; P = 0.016) were found to be statistically significant risk factors. Mean duration of mechanical ventilation, NICU stay in days and number of endotracheal tube changes in VAP as compared to Non-VAP group was 14.8 vs. 5.7, 24.8 vs. 10.4, 4.53 vs. 1.27 respectively. This was also statistically significant. Multiple logistic regression analysis revealed that duration of mechanical ventilation (P = 0.006) and VLBW (<15000 grams) (P = 0.032) were only two single independent and statistically significant risk factors for development of VAP.

Endotracheal aspirate culture was positive in all 32 VAP cases (100%) and blood culture was positive in 13 (40.62%). Most common bacteria isolated from ETA was Klebsiella spp. (37.5%). This was followed by E. coli (21.8%), Acinetobacter (15.6%) and staphylococcus aureus (9.3%). Polymicrobial infection was seen in 6.25%. Citrobacter was also grown in 6.25%.

23 (23.95%) out of 96 neonates enrolled in study died during the study period. There were 9 (28.1%) mortalities in VAP group and 14 (21.8%) in non-VAP group, which was statistically insignificant (OR 1.40; 95% CI 0.53-3.70; P = 0.61).

DISCUSSION

Quantitative culture samples obtained with fiberopticbroncoscopy using the Protected Specimen Brushings (PSB) or the bronchoalveolar lavage (BAL) mark the objective diagnostic criteria of VAP.9 These methods have a specificity and sensitivity of greater than 95% in the diagnosis of VAP.10 Marquette et al. found that endotracheal aspirate (ETA) cultures could be used as a reliable alternative to PSB at the cut off value of $10^6$ CFU/ML. The technique of PSB and BAL were not available to us in our NICU. We therefore used endotracheal aspirate technique as a diagnostic tool for VAP. It is a simple, non-invasive and a cost effective technique.

Due to differences in diagnostic criteria and aseptic precautions in intensive care units the reported incidences of VAP vary. We recorded an incidence of 33.34% or 68.96 cases per 1000 days of mechanical ventilation which is quite high but typical of a NICU that has been established recently in a resource poor setting.

The incidence of VAP increases with decreasing birth weight and decreasing gestational age. Birth weight <1500 grams was independent and statistically significant (P = 0.032) risk factor in our study for predicting VAP. This is because of immature immune system of preterm and VLBW babies making them more vulnerable to hospital acquired infections.11 Duration of mechanical ventilation was also independent and statistically significant (P = 0.006). This calls for daily assessments of readiness to wean and use of weaning protocols.

Despite the fact that majority of children developed late onset VAP (mean duration of ventilation was more than 5 days), the common organisms isolated were Klebsiella followed by E. coli and Acinetobacter. Similar observations were made by S. Tripathi, et al. (2009);12 Park JH, et al.13 Abdul KadirBozaykut et al.14 and RamyaSrinivasan, J. Asselin, et al. (2009).15

In our study out of total 96 cases enrolled 23 babies died (23.95%), out of which 9 died in VAP group (28.12%) and 14 died in non-VAP group (21.87%). This was statistically insignificant (P = 0.61). Similar observations were made among others by Yuan TM, et al.16

In conclusion to reduce the incidence of VAP to zero, infection control professionals must implement a strategy that is based on an accurate knowledge of VAP rates at their healthcare facility, so as to approach the interventions with cost-effective preventive measures. A slew of measures may be required based on the prevalent modifiable risk factors and etiological organisms in their NICU.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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DOI: 10.5455/2349-3291.iTCP20150204