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RESEARCH PAPER

Effectiveness of Educational Intervention in Preventing Ventilator Associated Pneumonia in Neonatal Intensive Care Unit: A Cohort Study

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Abstract:

Background: Despite improvement in overall survival, neonatal period is not free of complications. Ventilator associated Pneumonia (VAP) is a serious complication and account for 6.8 - 32.2 % of healthcare associated infections among neonates.

Objective: The objective of the study was to document the effectiveness of an educational programme for neonatal intensive care (NICU) service provider in preventing occurrence of ventilator associated pneumonia in NICU.

Methods: It was a prospective cohort study compared with historical control taken from the hospital records. All neonates admitted to the NICU during 12 months period from May 2019 to April 2020 were enrolled. Prospective enrollment of ventilated baby after educational interventions was subjected to the VAP educational care bundle. Eligible neonates who spent more than 48 h on MV were followed up and monitored closely for the development of VAP. Detail history, thorough clinical examination, relevant investigation including chest radiography were carried out on all enrolled infants.

Results: A total of 54 neonates ventilated newborn, 41 met the inclusion criteria and were enrolled in the current study; 22 cases in pre-intervention phase and 19 cases in the post- intervention phase. Among enrolled mechanically ventilated newborn, 18 patients (18/41, 44%) developed at least single episode of VAP during the ventilated period. Baseline characteristics were comparable in both the groups. The primary indication of mechanical ventilation was sepsis related complications during both the phases (9/22, 41% and 8/19, 42.1%). Next to sepsis, perinatal asphyxia (5/22, 22.7%) was the indication of MV in pre-intervention period whereas respiratory distress syndrome (7/19, 36.8%) was the second leading causes of MV during post-intervention period. Significant reduction in VAP incidence rate was observed after implementation of VAP interventions, as 13/22, 59 % episodes of VAP were diagnosed in pre-intervention period compared to 5/19, 26.3% were diagnosed during implementation period. (p = 0.035). Non-significant reduction in mean duration of MV days was observed in the post-intervention period when compared to pre-intervention counterpart (7.23±4.48 days versus 5.16±2.77 days, p = 0.089). There was no significant reduction in NICU length of stay (13.05±8.16 versus 11.58±7.75 days in pre and post intervention period respectively, p = 0.56). The difference in overall mortality rates between the two phases were 15/22, 68.18% and 10/19, 52.63% respectively and found to be non-significant. Gram negative bacteria were the most commonly isolated micro-organisms, Acinetobacter was the leading causative pathogen.

Conclusion: It demonstrates that an educational program including bundle of infection control practice can reduce the occurrence of VAP during ventilation period. These educational programs for NICU care providers can be expanded to other NICU s of the country to prevent ventilator associated pneumonia.

Key words: Ventilator associated pneumonia, NICU, Health care associated infection, Educational intervention

Introduction:

Significant advancement in the neonatal intensive care (NICUs) has contributed markedly to the survival of sick neonate in the last decades. Despite improvement in overall survival, neonatal period is not free of complications. Ventilator-associated pneumonia (VAP) in ventilated newborn is one such complication.[1] Ventilator-associated pneumonia (VAP) is defined by the Center for Disease Control and Prevention (CDC) and National Healthcare Safety Network as new and persistent radiographic infiltrates and worsening gas

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exchange in infants who are ventilated for at least 48h and presence of 3 out of following criteria: temperature instability with no other recognized cause, leukopenia, change in the characteristic of respiratory secretions, respiratory distress and bradycardia or tachycardia.[2] VAP is a serious complication in neonates on mechanical ventilation and account for 6.8 - 32.2 % of healthcare associated infections among neonates.[3,4] Although the effect of VAP on health care costs is significant in developing world, there is paucity of study in comparison to developed part.[5,6]

The CDC has published guidelines for the prevention of VAP, which is mainly consisted of the 'bundle approach'. The 'bundle approach' is described as simultaneous application of several evidence-based preventive measures for better outcome of the ventilated neonates by reducing VAP.[7,8] Although the efficacy of one or more elements are based on only theoretical evidence or biologic plausibility but these VAP preventive strategies are being successfully and widely used in many NICU settings.[9]

Newborns are different in perspective of anatomy, physiology, underlying disease pathology. Moreover, neonates often require more invasive procedures compared with older children, prospective studies evaluating preventive strategies of VAP are mandatory for the demonstration of proven efficacy.[10] In Bangladesh, reported incidences of VAP ranges from 19-20.8% in two prospective studies conducted in NICU of the same study settings and Dhaka Shishu (Children) Hospital respectively.[11,12] Scarcity is expected substantiating the efficacy of VAP prevention strategies among these newborn care units. Therefore, the aim of the present study is to assess the effectiveness of evidence based preventive care bundles in reducing VAP in ventilated neonates in NICU of the tertiary care referral center.

Materials and Methods

This prosepective cohort study with historic control comparative study was carried out in the NICU from May 2019 to April 2020 at Bangabandhu Sheikh Mujib Medical University. It is a tertiary referral 31 bedded NICU with single high frequency ventilator, 3 conventional mechanical ventilators and 5 CPAPs. All neonates admitted to the NICU and who required MV for 48 hours or more were included consequtively as intervention arm. Data of ventilated neonates admitted 6 months prior project inception from May 2019 to October 2019 were collected from unit NNPD database. This historic cohort was designated as control arm. Neonates with a diagnosis of pneumonia at the time of enrollment, neonates with major congenital anomaly, who required MV for less than 48 hours or death within 48 hours were excluded from the study. Ethical approval was taken from the National Research Ethics Committee of the Bangladesh Medical Research Council.

Incidence rate of ventilator associated pneumonia and other relevant parameters of ventilated newborn were collected from hospital record prior to the project inception. Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs 48-72 hours or thereafter following endo-tracheal intubation, characterised by the presence of a new or progressive infiltrate in the chest radiogram, signs of systemic infection (fever, altered white blood cell count), changes in sputum characteristics, and detection of a causative agent .

CDC criteria for diagnosis of VAP are two or more serial chest radiographs with at least one of the followings: new or progressive and persistant infiltrateand consolidation, cavitation, pneumatocele in infants<1yrs. Clinical criteria includes worsening gas exchange (eg. O2 desaturations, increased oxygen requirements or increased ventilator demands) And at least three of the followings: (a) temperature instability with no other recognized cause (b) leucopenia (<4000WBC/mm^3) or leucocytosis (>15000WBC/ mm^3) and left shift (>10%bands) (c) new onset of purulent sputum or change in character of increased suctioning requirements (d) apnea, tachypnea, nasal flaring with retraction of chest wall or grunting (e) Wheezing, rales or rhonchi (f) cough (g) bradycardia (<100bpm) or tachycardia (>170bpm).

The project activity was started with the educational program for NICU health care provider. Educational program was continued for one month. All NICU health care provider including doctors, nurses and other health care professionals were taught on current practice of evidence based care for the prevention of VAP and how to apply the care to the newborn. This was accomplished by powerpoint presentations, video demonstration and practical session explaining how to diagnose and prevent VAP by evidence based care bundle. The VAP prevention strategies proposed to be applied in this study were: strict hand hygiene, minimizing ventilator days by daily assessments of

readiness for weaning from MV, the use of noninvasive ventilation, elevation of the head of bed 15–30°, minimizing re-intubations, residual gastric volume monitoring, oral care with normal saline, changing ventilator circuits if visibly soiled, and careful handling of water trapped in the expiratory limb of ventilator circuits. No ventilated newborn was enrolled during this one month intervention period. Adhernce to VAP preventive measures were ensured by regular observation by the consultants and individual patient VAP checklist filled up by the attending nurse and residents.

Ventilated newborn who required MV for 48 hours or more were recruited as study subjects during the implementation phase. VAP preventive care bundle of the educational program were applied to the entire enrolled neonate. Neonates were closely monitored, during the entire period of ventilation, for the appearance of any of the clinical or radiological criteria defined by CDC for VAP diagnosis. Ventilated infants who experienced a new onset of abnormal chest radiographs along with criteria for the clinical diagnosis was diagnosed as VAP. Endotracheal tube tip culture was sent for bacteriological confirmation in all the ventilated neonates.

Baseline characteristics of enrolled neonates were obtained from records including their demographic characteristics, gestational age (GA), birth weight, and diagnosis on admission. Complete physical examination was carried out in all enrolled neonates. Baseline chest radiography and repeat chest radiogram were performed for all ventilated neonates, and radiographies were repeated as required. Laboratory investigations including hemogram, sepsis workup, biochemicals, renal functions and arterial bold gas analysis were done as per unit protocol. Neonatal morbidities other than VAP were managed by the institutional protocol. All ventilated neonates received intravenous nutrition, perenteral nutrition and other medication as prescribes by the attending physician. Routine sedation was not being practiced in the study setting. Microbiological studies included blood cultures and endotracheal tube tip culture and in selective cases cultures of the water trapped in the ventilator circuits (VCs) and water from humidification chamber. Ventilated newborn was followed up until discharge or death. Data from both the control arm and study arm were compared.

Data management: Data were analysed using IBM SPSS software package version 20.0 (IBM Corp, Armonk, New York, USA). Comparisons between groups for categorical variables were performed using the ÷2-test. Student's t-test was used to compare two groups for normally distributed quantitative data. The significance of the obtained results was judged at the 5% level.

Results

A total of 54 neonates were ventilated during 12 months period from May 2019 to April 2020. Among 30 ventilated newborn during pre-intervention period 8 newborn were excluded (3 neonate expired with 48 hours of mechanical ventilation and 5 newborn required mechanical ventilation for less than 48 hours). Five babies out of 24 were excluded during the intervention period as 2 died within 48 hours of mechanical ventilation and 3 excluded as they required mechanical ventilator for less than 48 hours. Thus among 41 enrolled mechanically ventilated newborn, 18 patients (18/41, 44%) developed at least single episode of VAP during the ventilated period. The two groups were comparable in term of gender distribution, birth weight distribution, mode of delivery, place of delivery and requirement of bag mask ventilation (table I).

The primary indication of mechanical ventilation was sepsis related complications during both the phases (9/22, 41% and 8/19, 42.1%). Next to sepsis, perinatal asphyxia (5/22, 22.72%) was the leading cause of MV in pre-intervention period whereas respiratory distress syndrome (7/19, 36.8%) was the second leading causes of MV during post-intervention period. Other indications of putting the newborns' in mechanical ventilator were pneumonia, apnea, post-surgical complications, meconium aspiration syndrome, transient tachypnea of newborn and birth defects causing respiratory failure (table II).

Significant reduction in VAP incidence rate was observed after implementation of VAP interventions, as 13/22, 59% episodes of VAP were diagnosed in pre-intervention period compared to 5/19, 26.3% were diagnosed during implementation period. (p 0.035). Non-significant reduction in mean duration of MV days was observed in the post-intervention period when compared to pre-intervention counterpart (7.23±4.48 days in phase I versus 5.16±2.77 days in phase-II, $p = 0.089$). There was no significant reduction in NICU length of stay (13.05±8.16 versus 11.58±7.75 days in pre and post intervention period respectively, $p = 0.56$).

Table I: Baseline demographic and clinical characteristics of enrolled infant, (n = 41)

Characteristics	Before intervention (n =22) No. (%)	After intervention (n =19) No. (%)	*p* value
Gestational age category (%)			
≥37 wks	2 (9%)	3 (15.8%)	0.42
32-36 wk	10 (45.5%)	5 (26.2%)	
< 32 wks	10 (45.5%)	11 (58%)	
Gestational age (weeks) mean±sd	32.14±3.32	32.05±3.64	0.08
Birth weight category (%)	2 (9%)	3 (15.8%)	
≥2500 g	6 (27%)	3 (15.8%)	0.844
1500-2499 g	14 (64%)	13 (68.4%)	
<1500 g			
Birth weight (gram) mean±sd	1475±543	1637±1084	0.54
Gender (%)			
Male (%)	12(54.5%)	9 (47.3%)	
Female (%)	10(45.5%)	10 (52.7%)	0.647
Mode of delivery			
LSCS (%)	12(54.5%)	9 (47.3%)	0.647
NVD (%)	10(45.5%)	10 (52.7%)	
Place of delivery			
Inborn (%)	14 (63.7%)	9(47.3%)	0.295
Outborn (%)	8 (36.3%)	10(52.7%)	
Bag mask ventilation			
Yes (%)	6 (27%)	5 (26%)	0.87
No (%)	16 (73 %)	14 (74%)	
IUGR			
Yes (%)	7 (32%)	5 (26%)	0.69
No (%)	15 (68%)	14 (73%)	

LSCS-Lower segment caesarian section, IUGR- Intrauterine growth restriction, NVD- Normal vaginal delivery

The difference in overall mortality rates between the two phases were 15/22, 68.18% and 10/19, 52.63% respectively and found to be non-significant p value 0.30 (table III).

Table II: Primary indication of mechanical ventilation among enrolled infants, (n = 41)

Indication	Before intervention (n =22) No. (%)	After intervention (n =19) No. (%)
Sepsis	9 (41%)	8 (42%)
Perinatal Asphyxia	5 (23%)	1 (5.2%)
RDS4 (18.2%)	7(37%)	
Pneumonia	1 (4.5%)	1(5.2%)
Apnea	1 (4.5%)	0
TTN 1 (4.5%)	0	
MAS	1 (4.5%)	0
Birth defect causing respiratory distress	0	2 (10.5%)

VAP- ventilator associated pneumonia, MV- Mechanical ventilation, NICU- Neonatal intensive care unit, RDS- Respiratory distress syndrome, TTN- Transient tachypnea of newborn, MAS- Meconium aspiration syndrome

Table III: Ventilator Associated Pneumonia and outcome among enrolled infants, (n =41)

Characteristics	Before intervention (n = 22) No. (%)	After intervention n = 19 No. (%)	*p* value
VAP (%)	13 (59%)	5 (26.3%)	0.035
Duration of MV (days) mean±sd	7.23±4.48	5.16±2.77	0.089
MV> 5 days (%)	16 (73%)	10 (53%)	0.183
Length of NICU(days) mean±sd	13.05±8.16	11.58±7.75	0.561
Death (%)	15(68%)	10 (52.63%)	0.309

VAP ventilator associated pneumonia, MV- Mechanical ventilation, NICU- Neonatal intensive care unit

Culture proven sepsis was associated among 5/22, 22.7% of enrolled newborns in pre-intervention period and nearly similar distribution of culture positivity was documented during post intervention period 5/19, 26.2%. Acinetobacter was the leading causative pathogen throughout the study period followed by Klebsiella and pseudomonas. Staph aureus and candida species were found in single episode during pre and post intervention period respectively. Multidrug resistance organism were isolated in 4/5, 80% and 3/5, 60 % cases respectively (table IV).

Table IV: Organisms isolated from blood in enrolled newborn (n = 41)

Pathogen	Before intervention (n = 22) No. (%)	After intervention (n = 19) No. (%)	*p* value
Positive cultures (%)	5 (23%)	5(26%)	0.51
Acinetobacter	2	3	
Klebsiella	1	1	
Pseudomonus	1	0	
E. coli	0	1	
Staph aureus	1	0	
Candida species	0	1	
MDR (%)	4/5 (80%)	3/5 (60%)	0.55

MDR Multidrug resistance

Discussion

Neonatal intensive care advancements have improved survival of sick newborn. Ventilator associated pneumonia become a major challenge among the most sick babies requiring mechanical ventilation in NICU. It represents an important cause of morbidity and mortality in this high-risk population.[2] Developmental immaturity including greater permeability of the skin and mucus membrane, lower level of immunoglobulin, and decreased complement activity increases their susceptibility to hospital-acquired infection. Mechanical ventilation increases risk of colonization with pathogenic bacteria in the oro-pharynx and tracheobronchial tree. VAP occurs when colonized bacterial, viral or fungal pathogens enter the sterile lower respiratory tract and lung parenchyma.[5]

Overall incidence of VAP was 44% (18/41) among enrolled mechanically ventilated newborn. The reported incidence of VAP was 19% in a previous studies conducted in the same institution by Mannan et al

during 2012 to 2014.[11] Nearly similar incidence (20.8%) was demonstrated by Ghosh U K et al in his prospective study done in a tertiary care NICU of Bangladesh.[12] Possible explanation of these fewer incidences may be related to under reporting, under diagnosis and possibly misdiagnosed as late onset pneumonia because most of the NICU had no facility of portable X ray machine for the radiological confirmation of VAP.

Several studies have shown a reduction of VAP rate after implementation of a care bundle.[5-10]The efficacy of the educational program among NICU health care provider on VAP prevention care bundle may result in a greater improvement in the favorable outcome in terms of development of VAP. Educational program and VAP prevention bundle unit protocol implemented in the present work was associated with statistically significant reduction in VAP rates in the study setting. Significant reduction in VAP incidence rate was observed after implementation of VAP interventions (59% vs 26.3%, p 0.035) (table II). All preventive measures of this VAP unit protocol were derived from controlled trials or health institutes recommendations for adults, children or neonatal VAP prevention.[5-10] There is clear evidence that hand hygiene is the most important infection control intervention in all health care setting, but it is regarded as one of the most difficult strategy to sustain among health care providers. Gram negative organisms which colonize the ETT are frequently carried on the hands of the care-givers.[13,14] Extensive hand hygiene training sessions were conducted throughout the study period, 6-steps hand washing posters were displayed on all sinks, alcohol-based hand rub solution were placed at each bedside, and in the corridor and continuous monitoring and feedback were provided to the NICU care providers to improve compliance with hand hygiene. Contamination of ventilator circuit can also facilitate pathogenesis of VAP, thus collection in the tubing should be drained away regularly to prevent aspiration.[15] Center for Disease Control and Prevention (CDC) recommended for sterile reusable respiratory care equipment, sterile water in humidifier chamber, regular drainage of condensate from the breathing circuit and hand hygiene before and after contact with respiratory equipment. Changing the breathing circuit unless it is visibly soiled is not recommended by the CDC guidelines.[6]We followed the CDC strategies regarding ventilator care in our bundle. The use of non-invasive measures such as nasal CPAP and nasal prong ventilation may reduce VAP rate. In time–sequenced cohort studies, reducing days of mechanical ventilation by non-invasive respiratory support decreased VAP incidence.[16,17] In the current study, attending physician assessed the readiness of every mechanically ventilated neonate for weaning to NCPAP on daily base, and every effort was done to wean them as soon as possible. Weaning trial note and documentation was maintained by the attending physician. Center for Disease Control and Prevention (CDC) recommended a comprehensive oral hygiene program for mechanically ventilated patient.[6] A meta- analysis by Pineda and colleagues showed reduction in VAP among adult patients treated by decontamination with oral chlorhexidine.[18] As chlorhexidine gluconate is not approved for infants less than 2 months, mouth care with normal saline and oro-pharyngeal suction were included in the care bundle. The criteria defined by Foglia and his colleagues were used throughout the present study periods to ensure uniformity of the results.[9]

The lack of respiratory therapists, unavailability of isolation facility for culture proven sepsis, lack of barrier nursing and relatively low nurse-to-patient ratio in the NICUs of Bangladesh may explain high rate of sepsis due to multidrug resistance organism in the present study. Moreover, systematic, rigorous hospital acquired infection surveillance on a multicenter collaborative network level by NICUs in most developed countries is a major gap between developed country and middle income country's NICU settings. Non-significant reduction in mean mechanical ventilation days/case were achieved (7.23±4.48 days versus 5.16±2.77 days, p = 0.089) in the study neonates in the post-intervention period, an important goal especially in premature to reduce the hazards of MV in sick population. Similarly, decline in length of NICU stay was documented in the current study but the result was not significant (13.05±8.16 versus 11.58±7.75days in pre and post intervention period respectively, p = 0.56). Possible explanation may be the other factors and co-morbidities leading to prolonged hospital stay in these population.

The overall mortality rate showed a trend toward reduction during the post-intervention period when compared to pre-intervention counter-part, but didn't reach statistical significance. The difference in overall mortality rates between the two phases were 15/22,

68.18% and 10/19, 52.63% (*p* value 0.3) respectively (table III). As we did not match patient to detect adjusted attributable mortality, it is not possible to conclude that the reduction in mortality is attributable to the decrease in VAP rate.

Gram negative bacteria were the predominant pathogen among enrolled ventilated newborn in the current study. Similar finding was shown in Yuan and colleague work and Xie and team trial[20], while *Staphylococcus aureus* and *Pseudomonus aeruginosa* were the most frequently identified pathogen in VAP in western pediatric populations.[19-22] Culture proven sepsis was associated among 5/22, 22.7% of enrolled newborns in the current study in pre-intervention period and similar distribution of culture positivity was documented during post intervention period 5/19, 26.2%. Acinetobacter was the leading causative pathogen throughout the study period followed by Klebsiella and pseudomonas. The difference in bacterial pattern between this study and that reported from high income countries may be due to antibiotic practice variation, difference in the NICU settings and infection control program. Awareness of local microbiological surveillance data on hospital-acquired infection can improve the selection of appropriate therapy. Even-though, the incidence of VAP was reduced with bundle implementation in our NICU, there was no significant difference in the incidence of multi-drug resistant organisms. Multidrug resistance organism were isolated in 4/5, 80% and 3/5, 60% cases respectively. The small sample size and lack of simultaneous enrollment as a part of randomized controlled trial were the limitations of this study; we suggest that multicenter approaches are necessary to attain larger sample sizes and to evaluate feasibility/ cost-effectiveness. Finally, future longitudinal cohort studies are recommended to validate the current findings taking into consideration the rate or level of adherence during the program.

Conclusion

Educational intervention regarding preventive measures appears to be effective reducing frequency of ventilator associated pneumonia in NICU setting. It demonstrated that an educational programme including bundle of infection control practice can reduce the occurrence of VAP during ventilation period. These educational programmes for NICU care providers can be expanded to other NICUs of the country to prevent ventilator associated pneumonia.

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