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Research Paper

Neonatal Mechanical Ventilation: Indications and Outcome

Medical Science

KEYWORDS : indications for ventilation, complications of ventilation, predictors of mortality

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ABSTRACT

Background and Aims: Decreasing mortality in sick and ventilated neonates is an endeavor of all neonatologists. To reduce the high mortality in this group of neonates, identification of risk factors is important. This study was undertaken to find out the indications of ventilation and complications in ventilated neonates and also study possible predictors of outcome. Subjects: Age <1-month; mechanically ventilated; not having suspected metabolic disorders or congenital anomalies; excluding postoperative patients. Methods: Neonates consecutively put on mechanical ventilation during the study period (October 2013 to November 2015) were enrolled. Primary diseases of the neonates along with complications present were listed. Clinical and laboratory parameters analyzed to find the predictors of mortality. Results: Total 280 neonates were ventilated. 52.5% were male. Mean age, weight, and gestational age were 21 ± 62 h, 2120 ± 660.5g, and 33.2 ± 4.9 weeks, respectively. 160 (57%) neonates died. Respiratory distress syndrome (RDS) (26.7%), sepsis (26.7%), and birth asphyxia (12%) were the most common indications for ventilation. Weight <2000 g, gestation <32 weeks, presence of sepsis, apnea, shock, hypoglycemia, neutropenia, and thrombocytopenia were significantly associated with mortality (P < 0.05). Resuscitation at birth, seizures, intra ventricular hemorrhage, or did not have a significant association with mortality. Conclusions: Weight <2000 g, gestation <32 weeks, shock, apnea, hypoglycemia, neutropenia, and thrombocytopenia were significant predictors of mortality in ventilated neonates.

INTRODUCTION

Advances in perinatal and neonatal care have significantly reduced neonatal morbidity and mortality rates. Outcome in sick infants has improved significantly, mostly due to more effective newborn intensive care. It is the introduction of widespread mechanical ventilation in the neonatal Intensive Care Units (NICU) [1] and its judicious use since, which has revolutionized the outcome and survival of sick newborns. [2] A significant proportion of neonates admitted to NICU require mechanical ventilation; and mechanically ventilated neonates have a high fatality. Various studies in developing countries have shown a mortality rate in the range of 40-60% [6],[7] in ventilated babies. Despite the availability of mechanical ventilation, mortality is still high in sick neonates. So to improve the mortality in ventilated neonates, identification of bad prognostic factors, and their remedy becomes mandatory. The primary aim of the present study was to find the risk factors responsible for poor outcome in ventilated neonates. We studied numerous clinical, biochemical, and hematological parameters in ventilated neonates and tried to relate them to outcome.

MATERIAL & METHODS

This retrospective study was conducted from October 2013 to November 2015 in the NICU of A J Institute of Medical Sciences. All neonates (aged 0-28 days) who required ventilation during the study period were eligible for inclusion in the study.

Neonates who had congenital anomalies or suspected metabolic disorders or postsurgical babies were excluded from the study; Clearance was taken from the local ethical committee. Informed consent was obtained at the same time from the parents/caregivers of every included neonate. For each ventilated neonate information, including age, sex, admission, weight (recorded by electronic weighing machine), gestational age (by modified Ballard's scoring), any maternal illness, type of delivery, any resuscitation at the time of birth, neonatal problems, primary diagnosis, hospital stay, and complications were recorded. The indications for initiation of mechanical ventilation were: (i) PaO_2 <50, (ii) $PaCO_2$ >60 mmHg, (iii) recurrent apnea, (v) poor respiration, (vi) O_2 saturation <85% on supplemental oxygen, (vii) continuous positive airway pressure (CPAP) failure, defined as worsening respiratory distress, and/or hypoxemia (PaO_2 <50 mmHg)/hypercarbia ($PaCO_2$ >60 mmHg) despite CPAP pressure of 7-8 cm H_2O. [8] Synchronized intermittent mandatory ventilation mode was the main mode of ventilation in the neonates in our study. Arterial blood gases were analyzed regularly. In general, the parameters were: Tidal volume 6-10 ml/kg, positive end-expiratory pressure 4-8 mmHg, peak inspiratory pressure 18-28 mmHg, inspiratory time 0.25-0.5 s, and FiO_2 0.40-0.80. Relevant investigations such as complete blood counts, chest X-ray, kidney function test, liver function test, blood culture, cerebrospinal fluid analysis, blood sugar, serum calcium, cranial ultrasound, etc., were done and repeated as needed. All neonates with positive blood culture or diagnosed with pneumonia, meningitis, or urinary tract infection were considered to have sepsis.

Shock was defined by clinical evidence of hypoperfusion in form of delayed capillary refill time (>3 s), oliguria (urine output <1 ml/kg/h), weak peripheral pulses, and hypotension.

Thrombocytopenia was defined as platelet count <150,000/µl. [10] . C-reactive protein (CRP) levels >6 mg/dl were taken as positive. Hypoglycemia was defined as blood sugar <40 mg/dl. The data was recorded on Microsoft Excel Worksheet and analyzed by GraphPad Instat 3.1 statistical program. Continuous variables were tested for normality using Kolmogorov and Smirnov method and Student's *t*-test, and Mann-Whitney U-test were used for comparison of normally distributed and nonparametric variables, respectively. Chi-square test and Fischer's exact test were used for categorical variables. $P < 0.05$ was considered significant. Those risk factors that were significant on univariate analysis ($P <$ 0.05) were entered into a forward step-wise multivariable

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logistic regression model and independent risk factors were determined.

RESULTS:

During the study, 945 neonates were admitted in total, out of which 280 were included in the study. 147 (52.5%) were male and 133 (47.5%) were female. Respiratory distress syndrome (RDS) (26.7), sepsis (26.7%), and meconium aspiration (15.7%) were the most common indications for ventilation [Table 1]. All the preterm neonates with gestational age <32 weeks or recurrent apneas or early features of RDS were given nasal CPAP therapy, and those who had a failure of nasal CPAP therapy were ventilated. Overall mortality in NICU during the study period was 15% and mortality in ventilated neonates was 57% (160/280).

Table 1: Indications for ventilation.

Indications for ventilation **	Number of patients (%)	Mortality (%)
Respiratory distress Syndrome	75(26.7)	46(61.3)
Sepsis	75(26.7)	52(69.3)
Birth asphyxia	30(10.7)	17(56.6)
Meningitis	18(0.06)	5(27.7)
Meconium aspiration	44(15.7)	27(61.3)
Pneumonia	20(0.07)	8(40)
Recurrent apnea	18(0.06)	5(27.7)

Table 2: Predictors of mortality in ventilated neonates

Parameter	Non survivors	Survivors	p values
Birth weight (kg)	1850+/-660.5	2450+/-750	0.03*
Gestational age (weeks)	33.3+/-3.9	36.2+/-2.8	0.04*
Age at admission (h)	2	3	0.1003**
Maternal age (years)	29(22-38)	30(20-36)	0.909**

(*Student's *t*-test used; **Mann–Whitney U-test used)

Among continuous variables studied, birth weight, gestational age, and differed significantly between ventilated neonates who survived and those who died ($P < 0.05$). Maternal age, age at admission, did not differ significantly in the two groups [Table 2].

Table 3: Predictors of Mortality in ventilated neonates

Parameters	Group 1			Group 2			p value
	Value	No	Mortality	Value	No	Mortality	
Birth weight(kg)	<2	178	78	>2	108	40	0.001
Gestational age (weeks)	<32	140	54	>32	140	52	<0.0001
Resuscitation at birth	yes	80	32	no	200	84	0.034
Apnea	present	68	26	absent	212	76	<0.0001
Birth asphyxia	yes	54	12	no	226	90	0.132
RDS	yes	75	20	no	205	62	0.045
MAS	yes	44	23	no	236	76	0.055
Pneumonia	yes	20	15	no	260	88	0.16
Sepsis	yes	75	43	no	205	49	<0.0001
Meningitis	yes	18	9	no	262	52	<0.0001
Hypoglycemia	yes	10	3	no	270	86	021
IVH	yes	15	4	no	265	42	0.43
CRP	positive	75	45	negative	205	44	0.009
Neutropenia	present	66	32	absent	214	84	<0.001
Thrombocytopenia	present	60	22	absent	220	82	<0.0001

(CRP –C Reactive Protein, VAP – Ventilator Associated Pneumonia, MAS – Meconium Aspiration Syndrome, RAS – Respiratory Distress Syndrome)

Among categorical parameters studied, birth weight <2 kg, prematurity <32 weeks, apnea, sepsis, shock, hypoglycemia, neutropenia, thrombocytopenia, and initial were significantly associated with mortality. Resuscitation at birth, birth asphyxia, RDS, MAS, pneumonia, meningitis, seizures, intraventricular hemorrhage (IVH), elevated CRP and had no significant relationship with mortality

DISCUSSION

Mortality among sick neonates in NICU is high, [12] but mortality among mechanically ventilated neonates and outborn neonates referred for ventilation is even higher. [2],[13],[14],[15] In this study, mortality in ventilated neonates was 43.3%, which is comparable to mortality of 46% reported by Sangeeta *et al*. [16] Hossain *et al*. [17] and Mathur *et al*.[15] reported higher figures of 70.6% and 74%,respectively. Sex and age at admission did not have a statistically significant association with the outcome as was found by Kollef [18] and Riyas *et al*. [6]

The outcome was however affected by the gestational age and birth weight of the neonate. Impact of low birth weight and prematurity on survival of neonates is known and reported by Mathur *et al*.[15] and Hossain *et al*. [17] as well.

We did not find a statistically significant difference in the mortality of neonates who were resuscitated as compared to those who were not resuscitated. It is a known fact that only cases of severe perinatal asphyxia have a high mortality and outcome is good in cases of mild and moderate perinatal asphyxia. Improved resuscitative measures at the time of birth and early referral for such babies seem to have led to the improvement in survival of all resuscitated .

Survival rate in our neonates for perinatal asphyxia and RDS was comparable to Hossain *et al*. [17] and Anantharaj and Bhat [19] . We saw a dismal outcome in neonates with sepsis. We had a survival rate of merely 35.3%. Respiratory failure and need for mechanical ventilation in a septic neonate signifies severe advanced disease and is a bad prognostic indicator. Pulmonary hemorrhage is a life threatening event in neonates and prognosis was dismal in our patients with this complication. Karthikeyan and Hossain [4] and Anantharaj and Bhat [19] also found a very poor outcome in neonates following pulmonary hemorrhage. Shock had a significant impact on mortality in ventilated neonates in our study. Anantharaj and Bhat [19] reported shock as the most common complication in ventilated neonates and also an important cause of mortality in their study. Shock represents an advanced stage of a disease process of varied etiologies and its relationship with mortality is understandable. Hypoglycemia is common in sick neonates and predicted increased mortality in our study. Association of hypoglycemia with poor neurological outcome is well known, but we also saw poor survival in hypoglycemic ventilated neonates. It needs to be kept in mind that hypoglycemia was not the primary cause of death in all of these neonates

Neutropenia and thrombocytopenia had a statistically significant correlation with mortality in our patients. Prognos-

tic significance of these parameters has been recognized by others as well. [21],[22],[23] . A lower pH at admission indicates a larger time gap between the onset of events leading to the deterioration in the clinical status of the child and presentation to the healthcare facility. Thus, it will definitely have an impact on the outcome of the patients.

Limitations

Our study did not focus on the proportion of patients receiving noninvasive ventilation/CPAP who subsequently needed intubation and mechanical ventilation. Furthermore, we were not able to study the factors determining the morbidity such as duration of NICU stay, mechanical ventilation, and hospital stay.

CONCLUSION:

Identification of risk of fatality in ventilated neonates is compulsory in order to intervene early, decrease the mortality, and even for triage in resource limited settings. Among the numerous commonly available variables studied by us, weight <2000 g, gestation <32 weeks, apnea, hypoglycemia, neutropenia, and thrombocytopenia were significant predictors of mortality in ventilated neonates.

REFERENCES

1. Carlo WA, Martin RJ. Principles of neonatal assisted ventilation. Pediatr Clin North Am 1986;33:221-37.
2. Singh M, Deorari AK, Paul VK, Mittal M, Shanker S, Munshi U, *et al.* Three-year experience with neonatal ventilation from a tertiary care hospital in Delhi. Indian Pediatr 1993;30:783-9.
3. Trotman H. The neonatal intensive care unit at the University Hospital of the West Indies: The first few years' experience. West Indian Med J 2006;55:75-9.
4. Karthikeyan G, Hossain MM. Conventional ventilation in neonates: Experience from Saudi Arabia. Indian J Pediatr 2002;69:15-8.
5. Richardson DK, Gray JE, Gortmaker SL, Goldmann DA, Pursley DM, McCormick MC. Declining severity adjusted mortality: Evidence of improving neonatal intensive care. Pediatrics 1998;102(4 Pt 1):893-9.
6. Riyas PK, Vijayakumar KM, Kulkarni ML. Neonatal mechanical ventilation. Indian J Pediatr 2003;70:537-40.
7. Kambarami R, Chidede O, Chirisa M. Neonatal intensive care in a developing country: Outcome and factors associated with mortality. Cent Afr J Med 2000;46:205-7.
8. M. Jeeva Sankar, Jhuma Sankar, Ramesh Agarwal, Vinod Paul, Ashok Deorari. Protocol for Administering Continuous Positive Airway Pressure in Neonates. AIIMS Neonatology Protocols 2014. Available from: URL: http://www.newbornwhocc.org/pdf/cpap_310508.pdf.
9. Niederman MS, Craven DE. Guidelines for the management of adults with hospital acquired, ventilator associated, and healthcare associated pneumonia. Am J Respir Crit Care Med 2005;171: 388 416. Available at: URL: https://www.thoracic.org/statements/resources/mtpi/guide1-29.pdf
10. Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I. Reference values for neutrophilic cells. J Pediatr 1979;95:89-98.
11. Mouzinho A, Rosenfeld CR, Sánchez PJ, Risser R. Revised reference ranges for circulating neutrophils in very-low-birth-weight neonates. Pediatrics 1994;94:76-82.
12. Arafa MA, Alshehri MA. Predictors of neonatal mortality in the intensive care unit in Abha, Saudi Arabia. Saudi Med J 2003;24:1374-6.
13. Nangia S, Saili A, Dutta AK, Gaur V, Singh M, Seth A, *et al.* Neonatal mechanical ventilation – Experience at a level II care centre. Indian J Pediatr 1998;65:291-6.
14. Mathur NC, Kumar S, Prasanna AL, Sahu UK, Kapoor R, Roy S, *et al.* Intermittent positive pressure ventilation in a neonatal intensive care unit: Hyderabad experience. Indian Pediatr 1998;35:349-52.
15. Mathur NB, Garg P, Mishra TK. Predictors of fatality in neonates requiring mechanical ventilation. Indian Pediatr 2005;42:645-51.
16. Sangeeta ST, Rajesh KC, Anurakti S. Study of early predictors of fatality in mechanically ventilated neonates in NICU. Online J Health Allied Sci 2009;8:3-9. Available from: URL: http://www.ojhas.org/ issue31/2009-3-9.htm.
17. Hossain MM, Mahfuza S, Abdullah MA, Hassan MN, Sahidullah M. Predictors of mortality in ventilated neonates in intensive care unit. Bangladesh J Child Health 2009;33:77-82.
18. Kollef MH. Do age and gender influence outcome from mechanical ventilation. Heart Lung 1993;22:442-9.
19. Anantharaj A, Bhat BV. Outcome of neonates requiring assisted ventilation. Turk J Pediatr 2011;53:547-53.
20. Basu S, Rathore P, Bhatia BD. Predictors of mortality in very low birth weight neonates in India. Singapore Med J 2008;49:556-60.
21. Baley JE, Stork EK, Warkentin PI, Shurin SB. Neonatal neutropenia. Clinical manifestations, cause, and outcome. Am J Dis Child 1988;142:1161-6.
22. Ballin A, Koren G, Kohelet D, Burger R, Greenwald M, Bryan AC, *et al.* Reduction of platelet counts induced by mechanical ventilation in newborn infants. J Pediatr 1987;111:445-9.
23. Qazi I, Charoo B, Ahmad A, Sheikh M, Baba AR. Thrombocytopenia and other haematological parameters in culture positive neonatal sepsis and their impact. J Pediatric Infect Dis 2013;8:25-9.