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Outcome of Neonatal Respiratory support Modalities in Sohag University Hospital

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ABSTRACT

Background: Preterm neonates are at high risk of developing respiratory distress in the immediate post-natal period. Traditionally, these infants are managed by intubation and mechanical ventilation. The use of continuous positive airway pressure (CPAP) has gained immense popularity as a primary mode of respiratory support in these infants.
Objective: To analyze indications of respiratory support, complications associated with each modality of respiratory support and short-term outcome.
Patients and methods: This study included 100 neonates admitted to NICU, Pediatrics Department, Faculty of Medicine, Sohag University Hospital during one-year period. Their age ranged from 0-28 days with symptoms of respiratory distress, which were evident shortly after birth and requiring respiratory support.
Results: The most common causes of admission were respiratory distress syndrome (RDS) 50%, sepsis 38%, asphyxia 8% and pneumonia 4%. Seventy two percent of the studied patients underwent CPAP, 14% oxygen support by nasal cannula and 14% mechanical ventilation. 82% of patients put on CPAP had improved and the failure rate of CPAP therapy was 18%. Adverse effects had occurred in 6 patients (42%) as: pneumothorax, ventilation acquired pneumonia and pulmonary hemorrhage. Mortality rate in ventilated babies in this work was 42.9%. Overall mortality rate in our study was 7%.
Conclusion: CPAP was the most widely used and safe modality of respiratory support.
Keywords: Neonates, Continuous positive airway pressure, NICU.

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 and aggressive respiratory and cardiovascular support [(1)].

Several different methods for respiratory support can be applied in the care of individual neonates. These methods include oxygen therapy, CPAP, invasive mechanical ventilation. Adequate tissue oxygenation maintenance is one of the primary goals of therapy during respiratory support. The simplest way to achieve adequate oxygenation is to increase the fraction of oxygen in inspired gas. However, oxygen must be considered a drug, because it has potential harmful side effects, such as retinopathy of prematurity and bronchopulmonary dysplasia (BPD) [(2)].

Continuous positive airway pressure (CPAP) has become a standard part of ventilatory care. It is believed to progress alveolar recruitment, inflate collapsed alveoli, and reduce intrapulmonary shunt. Application of CPAP appears to produce a more regular breathing pattern in preterm neonates and has been thought to be mediated through chest-wall stabilization and reduction of thoracic distortion. With excessive CPAP, however, the volume of the lung increases excessively, and the lung becomes over distended. Continued excessive CPAP may lead to very serious consequences, such as air leak syndromes. It may also increase dead space ventilation, leading to a rise in $PaCO_2$. High levels of CPAP can lead to a reduction in cardiac output, reduced pulmonary perfusion, and enhanced ventilation–perfusion (V/Q) mismatching, resulting in a lower PaO_2 [(3)].

The introduction of invasive ventilation for neonatal pulmonary insufficiency has resulted in the successful treatment of many previously fatal diseases. In addition, the refinement of mechanical ventilation during the past three decades has dramatically improved survival of many high-risk neonates. Moreover, the introduction of surfactant and total parenteral nutrition (TPN) has markedly impacted on this fall in neonatal mortality. Invasive mechanical ventilation can be indicated in a newborn gasping or with poor respiration, $PaO_2 < 50$ mmHg, $PaCO_2 > 60$ mmHg, oxygen saturation < 85% on supplemental O_2, intractable or recurrent apnea and CPAP failure [(4)].

Despite advances in the prevention and management of respiratory distress syndrome (including the widespread use of antenatal steroids and surfactant treatment), neonatal chronic lung disease is still one of the major complications in mechanically ventilated premature infant. This disease is seen in large preterm infants with severe respiratory distress syndrome who had been treated with high inspired oxygen concentrations and prolonged mechanical ventilation with high positive airway pressures [(5)].

Mortality is still high in sick neonates despite availability of mechanical ventilation. Various studies in developing countries have shown a mortality rate in the range of 40–60%. Common causes of neonatal deaths include sepsis, prematurity/LBW (especially VLBW preterm babies), birth asphyxia and congenital anomalies. So, identification of risk factors is important to reduce the mortality in this group [(6)].

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The aim of our study was to outline the indications of respiratory support in our NICU, complications associated with each modality of respiratory support and short-term outcome.

PATIENTS AND METHODS

This prospective observational study included 100 neonates admitted to NICU of Sohag University Hospital during one-year period.

Ethical and patients' approval: The study was approved by the Local Ethical Committee, Faculty of Medicine, Sohag University. Informed written consents were obtained from the parents.

Inclusion and exclusion criteria:

The study included neonates of either sex with age between 0 and 28 days with symptoms of respiratory distress (tachypnea, intercostal and subcostal retractions, nasal flaring and grunting) requiring respiratory support. Admitted neonates with respiratory distress were excluded if they have congenital malformations affecting the cardio-respiratory system, chromosomal aberrations, depression at birth (Apgar score at 5 minutes of < 7), fetal hydrops and clinical or laboratory evidence of severe vital organ dysfunction, which cause irreversible damage.

Interventions:

Antenatal history including maternal diseases, maternal infection (STORCH infection), prolonged rupture of membranes >18 hours. Natal history including gestational age, neonatal sex, and mode of delivery. Clinical examination including general conditions of the baby, assessment of gestational age, assessment of Apgar score at 1 and 5 minutes and systemic examination. Data of respiratory support including indications, mode, hospital course, acute adverse events, and duration of respiratory support. Laboratory investigations including arterial blood gases, complete blood count with differential leucocytic count, C-reactive protein quantitative assay and blood sugar. Radiological evaluation with chest X-ray was analyzed. The outcome was assessed based on the incidence of complications of respiratory support, duration of hospital stay and mortality.

Procedures:

Eligible infants were allocated to one of three modalities; oxygen, CPAP, MV depending on the degree of RD. Mild to moderate respiratory distress was defined as FiO_2 requirement 21-30% to maintain SpO_2 between 88-93%, and an arterial pH >7.2 and $PaCO_2$ < 60 mmHg [7].

CPAP was delivered by CPAP system with humidifier using short binasal prongs as interface. CPAP was initiated at 5 cmH_2O and a flow of 6 L/min with FiO_2 21% to maintain SpO_2 between 88-93 %. CPAP pressure and FiO_2 were titrated to a maximum of 7 cmH_2O and 60%, respectively. A maximum of 8 L/min of flow was allowed. The criteria for weaning were: absence of respiratory distress (minimal or no retractions and respiratory rate between 40 and 60 per minute), and SpO_2 > 90% on FiO_2<30% and PEEP <5 cm H_2O. Weaning from CPAP used stepwise reduction of FiO_2 by 5% to 21% and CPAP to 4cm H_2O, followed by removal of CPAP prongs. Infants were diagnosed to have failed NCPAP and were started on MV when they: (a) remained hypoxic, i.e. SpO_2 < 88% despite FiO_2 > 60%, and flow rate > 6 L/min and PEEP > 7 cm H_2O for NCPAP. (b) Infants that had recurrent apnea (>3 episodes within 24 hours) or any episode of apnea requiring bag and mask ventilation.(c) Infants that had pH < 7.2, or $PaCO_2$ > 60 mmHg [7].

The indications for initiation of mechanical ventilation were PaO_2 < 50 mmHg, $PaCO_2$ > 60 mmHg, gasping or poor respiration, O_2 saturation < 85% on supplemental oxygen and continuous positive airway pressure (CPAP) failure [8]**.** Extubation was attempted when the babies showed clinical, radiological improvement, normal blood gas and reducing ventilator requirements (peak inspiratory pressure (PIP) around 15 cm H_2O, peak end expiratory pressure (PEEP) of 4 cm H_2O, ventilator rate of ≤ 25 per minute, and oxygen requirement of < 40% [9]**.** Extubation failure (EF) is defined as an inability to sustain spontaneous breathing and need for re-intubation within 24–72 h after extubation [10]**.**

Data of maternal variables including maternal complications, mode of delivery and antenatal steroids were collected. Gestational age was calculated based on mothers last menstrual period and/or early pregnancy ultrasound scan or New Ballard score [11]. Infant variables evaluated included birth weight, gestational age, resuscitation, X-ray chest, arterial blood gases and FiO_2 requirement at initiation of therapy [12].

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

Independent-samples t-test of significance was used when comparing between two means. Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters. The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value ≤ 0.05 was considered significant, < 0.001 was considered as highly significant and > 0.05 was considered insignificant.

RESULTS

Table (1): Distribution of the studied patients according to demographic characteristics

Demographic characteristic	N=100	%
Gender:		
Male	63	63
Female	37	37
Gestational age (weeks):		
Mean ± SD	33.98 ± 3.44	
Range	27 - 40	
Birth weight (gm):		
Mean ± SD	1580 ± 560	
Range	600 – 4440	
Maternal age (years):		
Mean ± SD	25.77 ± 5.6	
Median (Range)	29 (18 – 41)	
Age at admission (days):		
Mean ± SD	4.26 ± 7.78	
Median (Range)	30 minutes (30 minute – 28 day)	
Weight at admission (gm):		
Mean ± SD	1550 ± 53	
Median (Range)	1400 (1045 – 4440)	

The total number of admissions in NICU over one year was five hundred neonates. One hundred newborn infants were included in the study. Male represented 63% of the studied patients with gestational age from 27 to 40 weeks with mean 33.98 weeks. Birth weight ranged from 600 to 4440 gm with mean 1580 gm. Maternal age ranged from 18 to 41 years with mean 25.77 years. Age at admission ranged from 30 minutes to 28 days while weight at admission ranged from 1045 to 4440 gm (Table 1).

Table (2): Distribution of the studied patients according to natal history

Natal history	N=100	%
ROM:		
Normal	71	71
PROM (≥ 12 hours)	29	29
Duration of PROM (days):		
Mean ± SD	20.9 ± 30.18	
Median (Range)	7 (0.5 – 90)	
Color of amniotic fluid:		
Clear	98	98
Meconium	2	2
Mode of delivery:		
NSVD	38	38
CS	62	62
Multiple pregnancy:		
No	71	71
Yes	29	29
Types of multiple pregnancy:	**N=29**	
Twins	17	58.6
Triplet	9	31.1
quadriple	3	10.3

29% had PROM with duration ranged 0.5 to 90 days. Meconium stained amniotic fluid was present in 2% (Table 2).

Table (3): Distribution of the studied patients according to presence and cause of RD

Postnatal history	N=100	%
Respiratory distress: **Yes**	100	100
Causes of respiratory distress:		
Birt asphyxia	4	4
Sepsis	38	38
RDS	50	50
Pneumonia	8	8

Table (4): Distribution of the studied patients according type of initial respiratory

Respiratory support	N& (%)	Gestational age: Mean ± SD	Birth weight (gm): Mean ± SD	Outcome	
				Improved N(%)	Failed N(%)*
CPAP	72	33.31 ± 2.9	1449.31 ± 468.93	59 (81.7%)	13 (18.3%)
Oxygen support	14	35.64 ± 1.55	2442.86 ± 800.69	9 (64.3%)	5 (35.7%)
Mechanical ventilation	14	30.93 ± 3.81	1307.14 ± 579.41	8 (57.1%)	6 (42.9%)

*Failed means deteriorated and put on MV for CPAP patients, put on CPAP for oxygen supported patients and deteriorated and died for mechanically ventilated patients (Table 4).

Table (5): Gestational age and birth weight of cases according to the outcome of respiratory support

Respiratory Support	Improved		Failed	
	GA Mean ± SD	Birth weight Mean ± SD	GA Mean ± SD	Birth weight Mean ± SD
O2 therapy	37.22 ± 1.86	2611.11 ± 553.27	33.6 ± 4.72	2070 ± 352.85
CPAP	33.41 ± 3.18	1516.10 ± 292.02	30.62 ± 2.66	1150 ± 203.10
MV	32.12 ± 3.94	1237.5 ± 516.68	30.5 ± 4.5	1008.33 ± 142.88

Newborn infants with lower geatational age and lower birth weight required higher levels of respiratory support with worse outcome (Table 5).

Table (6): Distribution of the studied patients according to outcome

	N=100	%
Outcome:		
Died	6	6
Survived	93	93
Hospitalization Days: Mean ± SD	12.16 ± 8.35	

Days in NICU stay ranged from 2 to 35 days. Adverse effects occurred in 6 (43%) patients of the 14 mechanically ventilated patients. These were pneumothorax, ventilation acquired pneumonia and pulmonary hemorrhage. These six patients deteriorated and died by the end of the study (Table 6).

Table (7): Predictors of mortality

Demographic data	Outcome		P value
	Died N=7	Alive N=93	
Gender:			
Male	3 (42.9)	60 (64.5)	0.418
Female	4 (57.1)	33 (35.5)	
Age on admission (days):			
Mean ± SD	7.43 ± 7.63	4.02 ± 7.77	0.044*
Gestational age (weeks):			
Mean ± SD	33.3 ± 3.9	36.2 ± 2.8	0.0.002*
Birth weight (gm):			
Mean ± SD	1965 ± 660.5	2630 ± 750.3	0.03*
Maternal age (years):			
Mean ± SD	26.43 ± 6.6	25.72 ± 5.56	0.749
Resuscitation at birth:			
No	0(0)	41(81.7)	0.039*
Yes	7(100)	52(18.3)	
PH	7.18 (6.80-7.36)	7.24 (6.99-7.47)	0.0022*
PO_2	46(22-70)	46(22-94)	0.26
PCO_2	46(28-68)	52(24-80)	0.098
RD grade:			
I	0 (0)	4 (4.3)	
II	1 (14.3)	37 (39.8)	0.008*
III	3 (42.9)	47 (50.5)	
IV	3 (42.9)	5 (5.4)	

Out of the analyzed clinical and laboratory parameters we found that weight < 2500 gm, prematurity < 34weeks, resuscitation at birth, severe RD and low pH were associated with mortality (P < 0.05). Maternal age, sex, and initial blood gas values (PO2 , PCO2) did not differ significantly.

DISCUSSION

Respiratory distress is a common presentation in the newborn infant. The term is used to describe a constellation of easily observable physical signs, including rapid breathing, retraction, flaring of the nostrils, grunting sound on expiration and cyanosis [13]. Any sign of postnatal respiratory distress is an indication for immediate examination and diagnostic evaluation as time and appropriate therapy is essential to prevent ongoing injury and improve outcome [14].

Preterm neonates are at high risk of developing respiratory distress in the immediate post-natal period. Traditionally, these infants are managed by intubation and mechanical ventilation. The use of continuous positive airway pressure (CPAP) has gained immense popularity as the primary mode of respiratory support in these infants [15]. Clinicians aim to use non-invasive respiratory support to minimize the risk of complications. Respiratory distress may be treated with non-invasive ventilatory strategies, such as nasal continuous positive airway pressure (NCPAP) and early surfactant, which are known to reduce the lung inflammation and injury associated with mechanical ventilation (MV) and decrease the incidence of bronchopulmonary dysplasia (BPD) [16].

CPAP increases mean airway pressure, and the associated increase in functional residual capacity should improve ventilation-perfusion relationships and potentially reduce oxygen requirements [17]. Drawbacks with the use of NCPAP could be difficulties in maintaining the nasal prongs in the nostrils, granulation, ulceration, necrosis, nasal vestibular stenosis, nasal deformities, poor tolerance of the infant to the apparatus, and difficulties in positioning the neonate [18].

Invasive mechanical ventilation can become a lifesaving intervention for patients with respiratory and breathing difficulties. The term "invasive" is used if it involves any instrument penetrating via the mouth (such as an endotracheal tube) or the nose to serve as an artificial airway.[9] Invasive mechanical ventilation may be used during acute respiratory failure, weaning and for chronic respiratory failure when non-invasive ventilation is impossible to manage correctly. It can also be used as a mean to maintain patient's airway during a surgical procedure, such as intubation done in the ICU [(19)]. Despite a life-saving treatment, support may lead to bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP) and neurologic impairment as complications of therapy [(20)].

This study was conducted on 100 neonates admitted to NICU of Sohag University Hospital during one-year period with age of 0-28 days with symptoms of respiratory distress requiring respiratory support. The most common causes of admission were RDS 50%, sepsis 38%, asphyxia 8% and pneumonia 4%. Seventy two percent of the studied patients underwent CPAP, 14% underwent oxygen support by nasal cannula and 14% underwent mechanical ventilation. 82% of patients put on CPAP improved and the failure rate of CPAP therapy was 18%. Adverse effects occurred in 6 (43%) of the ventilated patients as pneumothorax, ventilation acquired pneumonia and pulmonary hemorrhage. Mortality rate in ventilated babies in this work was 43%. Overall mortality rate in our study was 7%.

In this study 100 cases were included with gestational age ranging from 27 to 40 week with mean of 33.98 ± 3.44 weeks, sixty-three (63%) were boys and thirty-seven (37%) were girls. **Iqbal *et al.*** [(5)] studied the indications of ventilation and complications in ventilated neonates with 180 (60%) males and 120 (40%) females.

Birth weight of our studied neonates ranged from 600 to 4440 gm with a mean of 1580 gm. The age at admission ranged from 30 minutes to 28 days while weight at admission ranged from 1045 to 4440 gm. Maternal age ranged from 18 to 41 years with a mean of 25.77 years.

Respiratory distress was present in all patients; the most common cause of admission was RDS (50%), sepsis (38%), asphyxia (8%) and pneumonia (4%). While **Iqbal *et al.*** [(5)] reported that RDS was 31.1%, sepsis was 22.7%, and birth asphyxia was 18%. These were the most common indications for ventilation.

In our study, we used oxygen by nasal cannula, CPAP and classic mechanical ventilation. In this work 72 % of the studied patients underwent CPAP, 14% underwent oxygen support and 14% underwent mechanical ventilation. We used oxygen with full-term and near-term neonates with tachypnea and used nasal CPAP with all preterm neonates with recurrent apneas or early features of RDS and those who had a failure of nasal CPAP therapy or had respiratory acidosis were ventilated. This is similar to the results of **Iqbal *et al.*** [(5)] in which all the preterm neonates with gestational age < 32 weeks or recurrent apnea or early features of RDS were given nasal CPAP therapy, and those who had a failure of nasal CPAP therapy were ventilated.

Eighty-two (82%) of patients put on CPAP improved and the failure rate of CPAP therapy was 18%. CPAP failure was defined as increased respiratory distress, increased FiO_2 requirements and apnea. In comparison with **Trifi *et al.*** [(14)] they found that success rate of CPAP was 93%. The higher failure rate in our study may be attributed to late presentation, associated sepsis and limited resources in an example of developing countries.

Stay in NICU ranged from 2 to 35 days with a mean of 12.16 ± 8.5 days. Regarding outcome in this study, overall survival rate in NICU during the study period was 93%. 82% of patients on CPAP improved, 64.3% of those on oxygen support improved and 57% of patients on MV improved.

Fourteen (14%) of cases included in our study needed mechanical ventilation and the majority of them were due to CPAP failure. Adverse effects occurred in 6 (43%) of them as: pneumothorax, ventilation-acquired pneumonia and pulmonary hemorrhage. They died by the end of the study. Mortality rate in ventilated babies in this work was 43%. In a study of **Iqbal *et al.*** [(5)]**,** they found that mortality in ventilated neonates was 43% (130/300).

In this study, we found that birth weight, gestational age, and initial pH, resuscitation at birth, degree of respiratory distress, age on admission and type of respiratory support differed significantly between neonates who survived and those who died ($P < 0.05$). Maternal age, sex, and initial blood gas values (PO2, PCO2) did not differ significantly.

CONCLUSION

CPAP is the most widely used modality of non-invasive respiratory support and there are different devices and ways of delivering CPAP in practice. 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 < 2500 g, gestation < 34 weeks, and recurrent apnea were significant predictors of mortality in ventilated neonates.

REFERENCES

1. **Singh M, Deorari A, Paul V *et al.* (1993):** Three-year experience with neonatal ventilation from a tertiary care hospital in Delhi. Indian Pediatr., 30: 783-9.
2. **McPherson A, Hittner H, Kretzer F (1986):** Retinopathy of prematurity. Toronto: BC Decker Inc, Pp: 225–234.
3. **Eber E (2001):** Paediatric origins of adult lung disease bullet 8: Long term sequelae of bronchopulmonary dysplasia (chronic lung disease of infancy). Thorax, 56 (4): 317-323.
4. **John E, Carlo W (2003):** Respiratory distress syndrome in VLBW infants: changes in management and outcomes observed by the NICHD Neonatal Research Network. Semin Perinatol., 27: 288–92.

5. **Iqbal Q, Younus M, Ahmed A *et al.* (2015):** Neonatal mechanical ventilation: Indications and outcome. Indian J Crit Care Med., 19 (9): 523-7.
6. **Kambarami R, Chidede O, Chirisa M (2000):** Neonatal intensive care in a developing country: Outcome and factors associated with mortality. Cent Afr J Med., 46: 205-7.
7. **Hegde D, Mondkar J, Panchal H (2016):** Heated humidified high flow nasal cannula versus nasal continuous positive airway pressure as primary mode of respiratory support for respiratory distress in preterm infants. Indian Pediatrics, 53: 129-133.
8. **Martin S, Duke T, Davis P (2014):** Efficacy and safety of CPAP in neonatal care in low and middle income countries: a systematic review. Arch Dis Child Fetal Neonatal Ed., 99: 495-504.
9. **Tobin M (2001):** Advances in mechanical ventilation. N Engl J Medi., 344: 1986-1996.
10. **Vendettuoli V, Bellu R, Zanini R *et al.* (2014):** Changes in ventilator strategies and outcomes in preterm infants. Arch Dis Child Fetal Neonatal Ed., 99: 321–324.
11. **Ballard J, Khoury J, Wedig K *et al.* (1991):** New Ballard Score, expanded to include extremely premature infants. J Pediatr., 119: 417-23.
12. **Battaglia F, Lubchenco L (1967):** A practical classification of newborn infants by weight and gestational age. J Pediatr., 71: 159-63.
13. **Ian L (2006):** Respiratory transition in infants delivered by caesarean section. Semin Perinatology, 30 (5): 269-304.
14. **Dudell G, Stoll B (2008):** The fetus and Neonatal infant. Respiratory tract disorders. In: Behrman RE, Kleigman RM, Jenson HB. Nelson textbook of pediatrics, 18th edition. Saunders, Pp: 728-752.
15. **Sweet D, Bevilacqua G, Carnielli V (2007):** European consensus guidelines on the management of neonatal respiratory distress syndrome. J Perinat Med., 35: 175–186.
16. **Blencowe H, Cousens S, Oestergaard M (2012):** National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet, 379: 2162–72.
17. **Diblasi R (2009):** Nasal continuous positive airway pressure (CPAP) for the respiratory care of the newborn infant. Respir Care, 54: 1209–1235.
18. **Trifi A, Abdellatif S, Ben Ismail K *et al.* (2018):** Cardiac Ultrasound Assessment during Ventilator-Withdrawal Process: A Comparative Cohort Study. EC Emergency Medicine and Critical Care, 2(2): 34-42
19. **Graziani L, Spitzer A, Mitchell D *et al.* (1992):** Mechanical ventilation in preterm infants: neurosonographic and developmental studies. Pediatrics, 90: 515–522.
20. **Fanaroff A, Stoll B, Wright L *et al.* (2007):** Trends in Neonatal Morbidity and Mortality for Very Low Birthweight Infants. American Journal of Obstetrics and Gynecology, 147: 1- 8.