



EFFECTS OF EARLY NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE IN PRETERM NEONATES WITH HYALINE MEMBRANE IN A TERTIARY CENTRE

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ABSTRACT **Introduction:** Hyaline Membrane Disease is the commonest cause of respiratory distress in preterm infants. Lower the gestation, higher is the incidence of RDS and early intervention of this condition is essential for the survival of the neonate. Thus this study was conducted to assess the effect of non-invasive approach in the form of early nasal NCPAP in the management of the babies with hyaline membrane disease.

Methodology: Prospective study conducted among all the preterm neonates who were put on NCPAP treatment in the period December 2014 to May 2016. Data was collected by assessing blood gas analysis and pulse oximetry and evaluating the Silvermann Anderson (SA) scoring. Collected information was compiled in Microsoft excel 2013 and analyzed in SPSS Vr. 11 (Trial) Software, using Chi square test and reported as frequencies and percentages.

Results: Total number of deliveries in the study period was 2598 and preterm births (<37 weeks) was 323 (12.42 p.c). Incidence of Hyaline Membrane Disease (HMD) in ASRAM medical college during the study period i.e., from December 2014 to May 2016 was determined to be 110. Incidence of HMD in neonates with gestational age between 28-34 weeks: 4.2%. NCPAP was administered to 50 babies from the period 0 to 6 hours. Success rate found among those 50 neonates treated was 80 p.c.

Conclusion: Use of early nasal NCPAP which is simple, non-invasive, has low capital outlay and does not require expertise, is the option for us where most places cannot provide invasive ventilation.

KEYWORDS : Continuous Positive Airway Pressure, Hyaline Membrane Disease, Lung alveoli, Preterm baby, Respiratory distress syndrome, Surfactant, Silvermann Anderson score.

INTRODUCTION:

Respiratory distress syndrome (RDS) (or) Hyaline Membrane Disease (HMD) is the commonest cause of respiratory distress in preterm infants. Deficiency of pulmonary surfactant is one of the most important factors contributing to the development of RDS¹. In immature lungs, the elevated surface tension resulting from surfactant deficiency leads to alveolar collapse at the end of expiration, atelectasis, uneven inflation and regional alveolar over distension. If untreated, this will result in epithelial injury and pulmonary edema which further interferes with surfactant function, producing the clinical picture of RDS. Lower the gestation, higher is the incidence of RDS, accounting for nearly 80% incidence in preterm infants with gestational age less than 28 weeks.

Despite new preventive strategies, neonatal RDS is still the leading cause of mortality and morbidity in Neonatal Intensive Care Unit². Intermittent positive pressure ventilation (IPPV) with surfactant is the standard treatment for this condition. The major difficulty with IPPV is that it is invasive, resulting in airway and lung injury. Continuous Positive Airway Pressure (NCPAP) is a noninvasive respiratory support option and means to avoid harmful effects of positive pressure ventilation.

Mortality was high when infants were less than 1500 grams or required ventilation before 24 hours of age^{3,4}. Therefore another method for improving oxygenation in infants with RDS was sought and in 1971 Gregory et al.⁵ used continuous positive airway pressure in the treatment of idiopathic respiratory distress syndrome. It was thought that application of NCPAP might overcome atelectasis and improve arterial oxygenation. If grunting is prevented by insertion of endotracheal tube, arterial oxygen tension (PaO₂) decreases; however when tube is removed and grunting is resumed and PaO₂ rises. This was welcomed as a missing link between the oxygen and ventilatory therapy with great enthusiasm.

Continuous Distending Pressure (CDP) has been used for the

prevention and treatment of RDS as well as prevention of apnea, and in weaning from IPPV. NCPAP results in progressive recruitment of alveoli, inflates collapsed alveoli and reduces intrapulmonary shunt^{6,7}. It increases the functional residual capacity (FRC) and in turn gaseous exchange. It reduces inspiratory resistance by dilating the airways. This permits a larger tidal volume for a given pressure, so reducing the work of breathing⁸.

Bubble NCPAP is a newer NCPAP delivering system. It is NCPAP delivered with an underwater seal. It was shown that NCPAP delivered by underwater seal causes vibration of the chest due to gas flow under water, which is transmitted to infant's airway. These vibrations simulate waveforms produced by high frequency ventilation⁹. Bubble NCPAP has also shown to reduce the need for intubation, mechanical ventilation¹⁰, postnatal steroids and trend towards decreased incidence of chronic lung disease¹¹. With an underwater blow off system, sufficient flow creates continuous bubbling from the end of the underwater tube, placed at a specified depth underwater, to ensure that circuit pressure is maintained. A comparison of underwater bubble endotracheal (ET) NCPAP with conventional ventilator derived (ET) NCPAP in preterm neonates suggests that such oscillation contributes to gas exchange⁷.

Controversies still exist in the early respiratory management of RDS in premature infants. Considering the invasive nature, higher cost and high risk of chronic lung disease, IPPV with surfactant therapy may not be the ideal intervention in resource limited setting like India. Even though early NCPAP therapy has shown to be successful in clinical trials in the management of RDS, studies documenting the outcome of early NCPAP therapy are very scarce India¹²⁻¹⁵.

Present study is a hospital based prospective study and aims to find the incidence of premature neonates (less than 37 weeks) in NICU at ASRAM Hospital, to find the incidence of Hyaline Membrane Disease (HMD) in premature neonates with gestational age between 28-34 weeks in NICU and to evaluate the effectiveness of early nasal NCPAP

in these premature neonates with Hyaline Membrane Disease and manage the babies with hyaline membrane disease with non-invasive approach in the form of early nasal NCPAP.

MATERIALS AND METHODS

Hospital based prospective study was conducted in Neonatal Intensive Care Unit, at Alluri Sitarama Raju Academy of Medical Sciences, Eluru between December 2014 to May 2016 (one and a half year). Clinically diagnosed HMD neonates born with a gestational age of 28-34 weeks were the subjects for this study. Babies requiring respiratory support were treated with early nasal Continuous positive airway pressure (CPAP) and their outcome was studied and compiled.

All Preterms with HMD were evaluated using Silvermann Anderson (SA) scoring, blood gas analysis and pulse oxymetry. Babies with SA score of >4 or requiring $FiO_2 > 0.4$ to maintain PaO_2 above 50-60 mm Hg were treated with early nasal CPAP and effectiveness was judged using SA scoring and blood gas analysis. If symptoms progress and FiO_2 requirement is >0.6 to maintain SpO_2 above 85%, babies were ventilated. The babies requiring respiratory support were treated with early NCPAP (within 6 hours of onset of respiratory distress) and studied prospectively from December 2014 to May 2016.

NCPAP was administered to the neonates at different duration after birth (0hrs – 6hrs). During this period, various parameters were studied that as mentioned below:

Treatment success when: NCPAP is successful when the saturation is $>85\%$; PaO_2 of 60-80 mm Hg, $PaCO_2$ of 25 to 45 mm Hg and pH of 7.3 to 7.4 with $FiO_2 < 0.6$ and baby has no respiratory distress. Treatment failure if, either $PO_2 < 50$ mm Hg or $PCO_2 > 60$ mm Hg with $FiO_2 > 0.6$ or Silverman Anderson (SA) score >6 or Recurrent apnea.

Data was collected based on gender who responded to NCPAP treatment and its effect on the babies was determined based on their gestation age, birth weight and the effectiveness of NCPAP based on time of initiation like, ideal duration to wean off from NCPAP. Respiratory distress syndrome was categorized based on X-rays which fall into mild, moderate and severe. The effect of NCPAP on the babies based on antenatal steroids.

Inclusion and exclusion criteria:

Preterm neonates born in ASRAM hospital between 28-34 weeks, neonates with RDS with onset in less than 6 hours of birth and neonates whose Amniotic fluid L/s ratio of <1.5 or negative gastric aspirate shake test or Skiagram of chest showing either poor expansion with air bronchogram or reticulogranular pattern or ground glass opacity were included in the study.

All term neonates, neonates with congenital malformations, Preterms born outside ASRAM Hospital, Babies with Meconium Aspiration Syndrome, Babies with Birth Asphyxia and Babies born to mothers receiving general anesthesia or phenobarbitone or Pethidine or any other drugs likely to depress the baby were excluded in the study.

STATISTICAL ANALYSIS:

After the completion of the study, collected data was analyzed using appropriate statistical methods to find out the effectiveness of early nasal NCPAP in the treatment of preterm infants with HMD. Babies treated with nasal NCPAP treatment were classified into two groups namely success and failure group and comparison between the two groups were carried out and analyzed using Chi square test and student's 't' test and reported as frequencies and percentages.

RESULTS:

Total number of deliveries was 2598 and preterm births (<37 weeks) was 323 (12.42 p.c). Incidence of Hyaline Membrane Disease (HMD) in ASRAM medical college during the study period i.e., from December 2014 to May 2016 was determined to be 110. Incidence of HMD in neonates with gestational age between 28-34 weeks: 4.2%. NCPAP was administered to 50 babies from the period 0 to 6 hours. The mean age for the administration of NCPAP was found to be 4.16 ± 1.639 hrs. The success rate of NCPAP was determined to be 80 p.c (table 1) and it was 75 p.c in males and 88.88 p.c in females (Table 2) which was not significant statistically ($X^2 = 1.38$; $df = 1$; $p > 0.05$).

Based on gestational age and outcome after using nasal NCPAP out of 50 babies, 12 belonged to the gestational age of 28-30 weeks with 41.6

p.c success and 58.30 p.c failure rate, 30 babies were between 31-32 weeks of gestational age with 93.30 p.c and 6.67 p.c success and failure rates respectively and the remaining 8 between 33-34 weeks of gestational age with success rate is 87.5 p.c and failure rate was 12.5 p.c. There was statistically significant difference between success and failure groups with respect to gestational age ($p < 0.001$). Higher the gestational age more was the success rate (table 3).

Based on birth weight, 4 babies had weight < 999 g with 75 p.c managed with early nasal NCPAP alone and 25 p.c failed in management, 36 of them weighed between 1000-1500 g were 80.5 p.c and 19.5 p.c success and failure rates respectively and remaining 10 were in > 1500 g, where success and failure rates were 80 p.c and 20 p.c respectively ($p > 0.05$). Success and failure rates are not significantly different with respect to birth weight (table 4).

Table-5 depicts effect of nasal NCPAP on SA score before and 6 hours after application of nasal NCPAP. Out of 16 babies who were in SA score 4, 31.2 p.c babies improved to score 2, 43.8 p.c babies to score 3 and remaining 25 p.c worsened to SA score of 6 and required ventilation. Out of 34 babies who had a score of ≥ 5 before nasal NCPAP, 5.9 p.c babies improved to score 2, 52.9 p.c babies improved to score 3, 23.5 p.c babies improved to score 4, 7.7 p.c babies deteriorated to score 6 and 2.9 p.c babies deteriorated to score of 7 after 6 hours of nasal NCPAP which was statistically significant with $p < 0.005$.

DISCUSSION:

The incidence of prematurity in the present study was 12.42 p.c as compared to the National Statistics of 10-12 p.c in India¹⁶. The incidence of HMD in this study was 4.2% out of total deliveries. According to NNPD 2002-03 report¹⁷ involving 151,436 intramural deliveries, the incidence of HMD in India was 1.3 p.c of all live births.

50 preterm babies with gestational age 28 – 34 weeks with HMD were treated with early nasal NCPAP. Out of 50, 40 babies (80 p.c) were effectively managed with early nasal NCPAP alone. Remaining 10 (20 p.c) had to be intubated and required more invasive mechanical ventilation. When compared to a study conducted by Kamperet al.¹⁸ and Urs et al¹⁹ showed 84 p.c and 80 p.c success rate in treatment respectively.

CONCLUSION:

In developing countries like India, there is high burden of prematurity and sub-optimal use of antenatal steroid administration resulting infrequent HMD. In the present study, prematurity is the commonest predisposing factor for HMD. Its incidence increases as gestational age decreases. Early nasal NCPAP is useful in Mild and Moderate grade HMD. It may not be a replacement for assisted respiratory support (ventilation) in severe HMD. Nasal NCPAP is found to be effective in babies of mothers who had received antenatal steroids. Nasal NCPAP is safe, inexpensive and effective means of respiratory support in HMD. Use of early nasal NCPAP which is simple, non-invasive, has low capital outlay and does not require expertise, is the option for us where most places cannot provide invasive ventilation.

LIMITATIONS:

- No control group was taken for comparative analysis of the efficacy.
- Proportion of babies below 28 weeks of GA is low, which limits the generalizability of the results.
- The role of many confounding factors could not be evaluated because of the limited sample size.

TABLE 1. OUTCOME OF NCPAP IN THE PRESENT STUDY GROUP

Total number of babies treated	Success	Failure
50	No. (%)	No. (%)
	40 (80)	10(20)

Table 2. OUTCOME OF BABIES ON NCPAP BASED ON GENDER

Gender	Success	Failure	Total
	No. (%)	No. (%)	No. (%)
Male	24 (75)	8 (25)	32 (64)
Female	16 (88.9)	2 (11.1)	18 (36)
Total	40 (80)	10(20)	50 (100)

$\chi^2=1.38$ $df=1$ $p>0.05$ Not significant

TABLE 3. OUTCOME OF BABIES ON NCPAP BASED ON GESTATIONAL AGE

Gestational age in weeks	Success	Failure	Total
	No. (%)	No. (%)	No.
28-30	5 (41.7)	7 (58.3)	12
31-32	28 (93.3)	2 (6.7)	30
33-34	7 (87.5)	1 (12.5)	8
Total	40 (80)	10 (20)	50

$\chi^2=14.50$ $df=2$ $p>0.001$ Highly significant

TABLE 4. OUTCOME OF BABIES ON NCPAP BASED ON BIRTHWEIGHT

Birth weight (gms)	Success	Failure	Total
	No. (%)	No. (%)	No.
< 999	3 (75)	1 (25)	4
1000- 1500	29 (80.5)	7 (19.5)	36
> 1500	8 (80)	2 (20)	10
Total	40 (80)	10(20)	50

TABLE 5. STATISTICAL ANALYSIS OF SASCORE

Total babies	SA NCPAP before Score	SA score after 6 hours after NCPAP				
		2 (%)	3(%)	4 (%)	6 (%)	7 (%)
16	4	5 (31.2)	7 (43.8)	0 (0)	4 (25)	0(0)
34	≥5	2 (5.90)	18(52.9)	8 (23.5)	5 (14.7)	1(2.9)
50	Total babies	7 (14)	25 (50)	8 (16)	9 (18)	1 (2)

$\chi^2=24.50$ $df=8$ $p<0.005$

REFERENCES:

- Avery ME, Mead J. Surface properties in relation to atelectasis and hyaline membrane disease. *AMA journal of diseases of children*. 1959; 97(5, Part 1):517-23.
- Whitsett JA, Pryhuber GS, Rice WR, Warner BB, Wert SE. Acute respiratory disorders. In: Avery GB, Fletcher MA, MacDonald MG (eds), *Neonatology: Pathophysiology and Management of the Newborn*, 4 ed. Philadelphia: J.B. Lippincott Company; 1994: 429-452.
- Cooke R, Lunding M, Lomholt RG et al. Respiratory failure in newborn. The technique and results of intermittent positive pressure ventilation. *Acta Ped Scand* 1967; 56: 498-508.
- Adamson TM, Collins LM, Dehan M et al. Mechanical ventilation in newborn infants with respiratory failure. *Lancet* 1968; 2: 227-31.
- Gregory GA, Kitterman JA, Phibbs RH et al. Treatment of the idiopathic respiratory-distress syndrome with continuous positive airway pressure. *N Engl J Med* 1971; 284: 1333-40.
- Chernick V. Continuous distending pressure in hyaline membrane disease: Devices, disadvantages and a daring study. *Pediatrics* 1973; 52: 114-15.
- Saunders RA, Milner AD, Hopkins IE. The effects of NCPAP on lung mechanics and lung volumes in the neonates. *Biol Neonate*. 1976; 29: 178-184.
- Harris TR, Wood BR. Physiologic Principles. In: Goldsmith JP, Karotkin EH eds. *Assisted Ventilation*, 3rd edn. Philadelphia; WB Saunders, 1996: 21-68.
- Locker R, Greenspan JS, Shaffer TS et al. Effect of nasal NCPAP on thoraco-abdominal motion in neonates with respiratory insufficiency. *Pediatr Res*. 1994; 11: 259-264.
- Lee US, Dunn MS, Fenwick M et al. A comparison of underwater bubble continuous positive airway pressure (NCPAP) with ventilator derived NCPAP in preterm neonates ready for extubation. *Biol Neonate* 1998; 73: 69-75.
- De Klerk AM, De Klerk RK. Use of continuous positive airway pressure in preterm infants: Comments and experience from New Zealand. *Pediatrics* 2001; 108: 761-2.
- Narendran V, Donovan EF, Hoath SB et al. Early bubble NCPAP and outcomes in ELBW preterm infants. *J Perinatol* 2003; 23: 195-199.
- Diblasi RM. Nasal continuous positive airway pressure (NCPAP) for the respiratory care of the newborn infant. *Respiratory care*. 2009; 54(9):1209-35.
- Sekar K. The role of continuous positive airway pressure therapy in the management of respiratory distress in extremely premature infants. *The journal of pediatric pharmacology and therapeutics: JPPT: the official journal of PPAG*. 2006; 11(3):145-52.
- Sekar KC, Corff KE. To tube or not to tube babies with respiratory distress syndrome. *Journal of perinatology: official journal of the California Perinatal Association*. 2009; 29(Suppl 2):S68-72.
- Meharban Singh. *Care of the Newborn*. 6th Ed., page. 219.
- Report of the National Neonatal Perinatal Database. *National Neonatology Forum, India*; 2002-03.
- Kamper J, Ringsted C. Early treatment of idiopathic respiratory distress syndrome using binasal continuous positive airway pressure. *Acta Paediatr Scand*. 1990; 79: 581-6.
- Prashanth S Urs, Firdose Khan, Maiya PP. Bubble NCPAP – A primary respiratory support for respiratory distress syndrome in newborns. *Indian Pediatrics* 2009; 46: 409-411.