

## Original Research Article

# Use of early nasal continuous positive airway pressure in preterm neonates with hyaline membrane disease (neonatal respiratory distress syndrome)

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### ABSTRACT

**Background:** In developing countries like ours, there is high burden of prematurity and sub-optimal use of antenatal steroid administration resulting infrequent hyaline membrane disease (HMD).

**Methods:** A total 50 cases of clinically diagnosed HMD with gestational age between 28-34 weeks admitted to neonatal intensive care unit (ICU). 50 babies were treated with early nasal continuous positive airway pressure (CPAP) (within 6 hours of onset of respiratory distress).

**Results:** Incidence of prematurity was 12.42%. Incidence of HMD observed between gestational ages of 28-34 weeks is 3.2%. Out of total 50 babies who were managed with early nasal CPAP, it proved effective in 40 babies (80%), remaining 10 babies (20%) had to be intubated and required ventilation. Out of 10 babies who required ventilation 90% of the babies were less than 32 weeks gestation age; remaining 10% were between 33-34 weeks. Analysis of these results showed that outcome is better with increased gestational age ( $p < 0.005$ ). Out of 10 babies who failed 80% were  $< 1500$  g and remaining 20% above 1500 g. We found significant improvement ( $p < 0.005$ ) in SA score after application of nasal CPAP. Babies on CPAP had significant improvement in oxygenation ( $p < 0.05$ ). A success rate of 93.1% observed in moderate grade HMD ( $p < 0.005$ ). Out of 10 babies who failed on nasal CPAP, 80% of them had severe grade HMD and 20% showed moderate HMD. A success rate of 92.86% was found in babies of mothers who had received antenatal steroids and 63.63% of babies whose mothers had not received antenatal steroids improved with early nasal CPAP ( $p < 0.05$ ).

**Conclusions:** Nasal CPAP is found to be effective in babies of mothers who had received antenatal steroids. Nasal CPAP is safe, inexpensive and effective means of respiratory support in HMD. Use of early nasal CPAP 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:** Respiratory distress syndrome, Preterm neonates, Hyaline membrane disease, Nasal CPAP

### INTRODUCTION

Respiratory distress syndrome (RDS) is the commonest cause of respiratory distress in preterm infants. Deficiency of pulmonary surfactant is one of the most important factor contributing to the development of RDS.<sup>1</sup> 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, results in epithelial injury and pulmonary edema which further interfere with surfactant function, producing the clinical picture of RDS.

Despite new preventive strategies, neonatal RDS is still the leading cause of mortality and morbidity in neonatal intensive care.<sup>2</sup> Intermittent positive pressure ventilation

(IPPV) with surfactant is the standard treatment for the condition. The major difficulty with IPPV is that it is invasive, resulting in airway and lung injury. Continuous positive airway pressure (CPAP) is a noninvasive respiratory support option and means to avoid harmful effects of positive pressure ventilation.

CPAP results in progressive recruitment of alveoli, inflates collapsed alveoli and reduces intrapulmonary shunt. It increases the final 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 breathing.<sup>3,4</sup> It regularizes and slows the respiratory rate. It increases the mean airway pressure and improves ventilation perfusion mismatch. It conserves surfactant on the alveolar surface.<sup>5-7</sup>

CPAP is applied via a face mask, nasopharyngeal tube, or nasal prongs, using a conventional ventilator, bubble circuit or CPAP driver. Application of positive compared with negative pressure might have different results in terms of effectiveness and complications.

Bubble CPAP is a newer CPAP delivering system. It is CPAP delivered by CPAP system with underwater seal. It has been shown that CPAP 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 ventilation. Bubble CPAP has also been shown to reduce need for intubation and mechanical ventilation, postnatal steroids and trend towards decreased incidence of chronic lung disease.<sup>8</sup>

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 CPAP therapy has been shown to be successful in clinical trials in the management of RDS, studies documenting the outcome of early CPAP therapy are very scarce INDIA.<sup>9-12</sup>

Present study is a hospital based study and aims at managing increased number of babies with hyaline membrane disease with non-invasive approach in the form of early nasal CPAP.

### **Objectives**

Objectives of the study were to find the incidence of premature neonates (less than 37 weeks) in our hospital, to find the incidence of hyaline membrane disease in premature neonates with gestational age between 28-34 weeks, and to evaluate the effectiveness of early nasal CPAP in these premature neonates with hyaline membrane disease.

## **METHODS**

The study was conducted at neonatal ICU, GIMSR Medical College Hospital, and OMNI RK Hospital Visakhapatnam from June 2019 to May 2020.

### **Collection of data**

50 neonates with hyaline membrane disease (HMD) clinically diagnosed with gestational age 28-34 weeks admitted to neonatal ICU were subjects for this study. The following symptoms were taken into account: preterm neonate, RDS having onset within 6 hours of birth, amniotic fluid I/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.

### **Exclusion criteria**

All term neonates, neonates with congenital malformations, babies born to mothers receiving general anesthesia, phenobarbitone, pethidine and other drugs likely to depress the baby, babies with meconium aspiration syndrome, and babies with birth asphyxia

### **CPAP treatment**

The babies requiring respiratory support were treated with early nasal CPAP (within 6 hours of onset of respiratory distress) and studied prospectively from July 2019 to May 2020. CPAP was administered to the neonates at different duration after birth (0 hours to 6 hours). During this period, various parameters were studied that are mentioned below. CPAP is successful when the saturation is >85%; PaO<sub>2</sub> of 60-80 mm Hg, PaCO<sub>2</sub> of 25 to 45 mm Hg and pH of 7.3 to 7.4 with FiO<sub>2</sub><0.6. Baby has no respiratory distress.

CPAP failure is defined as: PO<sub>2</sub> < 50 mm Hg or PCO<sub>2</sub>>60 mm Hg with FiO<sub>2</sub>>0.6; SAS score >6; and recurrent apnea.

### **Effect of CPAP on the gender**

Data was collected based on gender who responded to CPAP treatment.

### **Effect of CPAP on the babies based on gestation age**

The effect of CPAP on the babies was determined based on their gestation age.

### **Effect of CPAP on the birth weight of babies**

The effect of CPAP on the birth weight of the babies was studied.

### **Effectiveness of CPAP based on time**

The ideal duration to wean off from CPAP was determined among the study group.

### **Study on the respiratory distress in the babies based on SA score and ABG parameters**

Respiratory distress in the babies was assessed based on SA score and ABG parameters. 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.

### **X ray studies**

Respiratory distress syndrome was categorized based on X-rays which fall into mild, moderate and severe. The effect of CPAP on the babies based on antenatal steroids.

### **Statistics**

Proportions were compared using Chi-square ( $\chi^2$ ) test of significance. Proportion of cases belonging to specific group of parameter or having a particular problems was expressed in absolute number and percentage. The results were averaged (mean  $\pm$  standard deviation) for each parameter (duration of treatment, age at admission, age at treatment and ABG parameter) between the groups. Student's 't' test used to find a significant difference between two means.

## **RESULTS**

Total number of preterm neonates (<37 weeks): 503, incidence of preterm neonates: 12.42%; total number of diagnosed HMD cases: 130; incidence of HMD in neonates with gestational age between 28-34 weeks: 3.2%

### **Determination of the age for the administration of CPAP**

CPAP was administered to 50 babies from the period 0 hours to 6 hours. The mean age for the administration of CPAP was found to be  $4.16 \pm 1.639$  hours.

### **Outcome of the CPAP administration**

Among 50 babies, 40 improved with success rate of 80%, whereas 10 babies (20%) failed requiring higher mode of ventilation.

We found a success rate of 75% in males and 88.88% in females ( $p > 0.005$ ).

### **Outcome and gestational age**

In babies who were between 28-30 weeks < there is 41.67% success and 58.30% failure rate. Outcome in babies of 31-32 weeks gestation is 93.30% and 6.67% success and failure rates respectively. Among 33-34 weeks, success rate is 87.5% and failure rate is 12.5%.

There is statistically significant difference between success and failure groups with respect to gestational age ( $p < 0.001$ ). Higher the gestational age more is the success rate.

### **Outcome and birth weight (gm)**

Out of 50 babies, 4 belonged to <999 g, 36 in 1000-1500 g and remaining 10 were in >1501 g. In babies who were <999 g 75% were managed with early nasal CPAP alone and 25% failed. Outcomes in 1000-1500 g group were 80.5% and 19.5% success and failure rates respectively. In babies >1500 gm success and failure rates were 80% and 20% respectively ( $p > 0.05$ ). Success and failure rates are not significantly different with respect to birth weight (Table 1).

### **Effectiveness of CPAP based on time**

The mean duration in success group was  $38.5 \pm 15.4$  hours with range being 10-72 hours. Similarly mean duration of treatment in failure group was  $9.0 \pm 1.7$  hours range being 8-12 hours.

### **Study on the respiratory distress in the babies based on Silvermann Anderson (SA) score and arterial blood gas (ABG) parameters**

Before treatment, it was found that 61.2% were in score 5, 6% in score 6 and 32% in score 4. After 6 hours of CPAP administration, there was a change in the SA score where 40 babies showed a decrease in the score ( $\leq 4$ ) while the remaining showed an increase in the SA score. But after 12 hours, the study group has shown the SA score less than 4 indicating the improvement of the babies with CPAP (Table 2).

### **SA score before and 6 hours after application of nasal CPAP**

Out of 16 babies who were in SA score 4, 5 (31.2%) babies improved to score 2, 7 (43.8%) babies to score 3 and remaining 4 babies (25%) worsened to SA score of 6 and required ventilation.

Out of 34 babies who had a score of  $\geq 5$  before nasal CPAP, 2 (5.9%) babies improved to score 2, 18 (52.9%) babies improved to score 3, 8 (23.5%) babies improved to score 4, 5 (14.7%) babies deteriorated to score 6 and 1 (2.9%) baby deteriorated to score of 7 after 6 hours of nasal CPAP (statistically significant,  $p < 0.005$ ) (Table 3).

### **ABG analysis**

The ABG parameters involved in the respiratory distress syndrome was studied and analyzed statistically significant.

The various parameters taken into consideration were pH, PO<sub>2</sub>, PCO<sub>2</sub>, HCO<sub>3</sub> before and after CPAP. The results showed significant increase in oxygenation and bicarbonate as indicated by the p values. This indicates the positive effect of CPAP on the neonates (Table 4).

**X ray studies**

HMD grading was done based on X-rays. The different grades are mild, moderate and severe (Table 5).

The effectiveness of CPAP on babies with different HMD grading was assessed. It was found that 100 % efficiency was observed in mild HMD while 93% success was found in moderate HMD (statistically significant p<0.005). In severe grade HMD the success rate was only 46.67%. This

result therefore suggests the usefulness of CPAP in mild and moderate HMD babies.

**Effect of antenatal steroids**

Of the 50 babies studied, some of the mothers were on antenatal steroids. The babies were categorized on this basis and the effect of CPAP was studied and the results are provided below (Table 6).

It is found that success rate was 92.86% in babies of mothers who had received antenatal steroids, whereas only 63.63% of the babies improved whose mothers did not receive antenatal steroids (statistically significant p<0.05). Hence, antenatal steroids in mother had definite role in better outcome of HMD when treated with CPAP.

**Table 1: Outcome measurement in gender, gestational age, and birth weight.**

Parameter	Total	Success		Failure		P value
		Number	Percent	Number	Percent	
<b>Gender</b>						
Male	32	24	75	8	25	>0.05 (ns)
Female	18	16	88.88	2	11.11	
<b>Gestational age in weeks</b>						
28-30	12	5	41.67	7	58.33	>0.001* (sig)
31-32	30	28	93.30	2	6.67	
33-34	8	7	87.50	1	12.50	
<b>Birth weight (gms)</b>						
<999	4	3	75	1	25	>0.05 (ns)
1000-1500	36	29	80.5	7	19.5	
1501-2000	10	8	80	2	20	

**Table 2: SA scores and its effect.**

SA score	Before treatment		After 6 hours		After 12 hours	
	Number	Percent	Number	Percent	Number	Percent
1	-	-	-	-	13	32.5
2	-	-	7	14	26	65
3	-	-	25	50	1	2.5
4	16	32	8	16	-	-
5	31	61.2	-	-	-	-
6	3	6	9	18	-	-
7	-	-	1	2	-	-

**Table 3: Statistical analysis of SA score.**

Total babies	SA score before CPAP	SA score after 6 hours after CPAP (%)				
		2	3	4	6	7
16	4	5 (31.2)	7 (43.8)	0 (0.00)	4 (25.00)	0 (0.00)
34	≥5	2 (5.90)	18 (52.9)	8 (23.5)	5 (14.7)	1 (2.90)
50	Total babies	7 (14.00)	25 (50.00)	8 (16.00)	9 (18.00)	1 (2.00)

χ<sup>2</sup>=24.50, df=8, p<0.005.

**Table 4: Statistical analysis of ABG results.**

ABG parameter	Before early nasal CPAP (mean±SD)		After early nasal CPAP (mean±SD)	
	Success group	Failure group	Success group	Failure group
<b>pH</b>	7.268±0.079	7.314±0.1099	7.379±0.05	7.319±0.1188
't' value	1.4333		2.00	
'p' value	0.178		0.073	
<b>PO<sub>2</sub></b>	57.66±10.58	55.93±10.96	80.48±7.52	42.16±18.83
't' value	0.451		6.309	
'p' value	0.659		0.00*	
<b>PCO<sub>2</sub></b>	41.31±11.14	36.99±10.42	30.62±6.67	38.40±9.73
't' value	1.147		2.389	
'p' value	0.270		0.036*	
<b>HCO<sub>3</sub><sup>-2</sup></b>	18.377±0.97	18.56±0.81	20.507±1.149	17.15±0.83
't' value	t=0.64		10.82	
'p' value	>0.05		<0.001	

**Table 5: Effect of CPAP on babies categorized based on HMD.**

HMD grading	Total	Success		Failure	
		Number	Percent	Number	Percent
<b>Mild</b>	6	6	100.00	--	--
<b>Moderate</b>	29	27	93.10	2	6.9
<b>Severe</b>	15	7	46.67	8	53.33
<b>Total</b>	50	40	80.00	10	20.00

$\chi^2=6.5$ df=2, p<0.005.

**Table 6: Antenatal steroids and outcome.**

Steroids received	Total	Success		Failure	
		Number	Percent	Number	Percent
<b>Yes</b>	28	26	92.86	2	7.14
<b>No</b>	22	14	63.63	8	36.37
<b>Total</b>	50	40	80.00	10	20.00

$\chi^2=6.5$ , df =1, p<0.05.

## DISCUSSION

50 preterm babies with gestational age 28–34 weeks with HMD were treated with early nasal CPAP. Out of 50, 40 babies (80%) were effectively managed with early nasal CPAP alone. Remaining 10 (20%) had to be intubated and required more invasive mechanical ventilation. Kamper et al found success rate of 84% in HMD with CPAP system used with a binasal tube.<sup>13</sup>

In a study by Gitterman et al concluded that early nasal CPAP is an effective treatment of respiratory distress in VLBW infants, significantly reducing the need for intubation and intermittent mandatory ventilation without worsening other standard measures of neonatal outcome.<sup>14</sup>

The results were analyzed based on gender characteristics and found no statistically significant difference in the outcome between the two groups (p>0.005).

Out of 10 babies who required ventilation 90% of the babies were less than 32 weeks gestation age; remaining 10% were between 33–34 weeks. success rate of 75% in babies <999 g, 80.5% in 1000–1500 g and 80% in babies >1500 g. Aly et al studied outcome of nasal CPAP in ELBW.<sup>15</sup> Nasal CPAP management increased in the surviving infants over time, whereas the need for surfactant treatment decreased.

Effectiveness of early nasal CPAP was judged based on SA scoring and blood gas parameters. Out of 16 babies who were in SA score 4, 31.2% improved to score 2 and 43.8% to score 3 after 6 hours.

Remaining 4 babies (25%) who were in SA score 4 worsened to SA score 6 after 6 hours and had to be ventilated. Out of 31 babies who were in score 5 before early nasal CPAP, 6.4% improved to score 2, 58.1% to score 3 and 16.1% to score 4 after 6 hours. Remaining 6



babies (19.3%) in this group worsened to score >6 and failed. 3 babies were in score 6 before treatment. All of them improved to score 4 after 6 hours.

In our study we found that babies on CPAP had significant improvement in oxygenation ( $p<0.05$ ), other parameters varied. With this we could reduce  $FiO_2$  significantly and wean down the babies.

Grade HMD based on radiological appearance, 6 babies showed mild HMD. All of the improved on nasal CPAP (success rate of 100%). 29 babies belonged to moderate grade HMD. We found a success rate of 93.1% in this group ( $p<0.005$ ).

Out of 10 babies who failed on nasal CPAP, 80% of them had severe grade HMD and 20% showed moderate HMD. With this we conclude that early nasal CPAP is effective in mild and moderate HMD. It may not be a replacement for assisted respiratory support (ventilation) in severe cases of HMD. Schmid et al showed that CPAP was an effective method in newborns with all grades except severe HMD.<sup>16</sup>

Our study found that 26 (92.86%) of 28 babies whose mothers had received antenatal steroids improved with nasal CPAP, whereas out of 22 babies whose mothers had not received antenatal steroids only 14 (63.63%) improved and 8 (36.37%) failed. Statistical analysis showed  $p<0.05$  (significant). Antenatal steroid administration helps us to predict the severity of HMD and need for invasive respiratory support. Study by Sandri et al., has shown trend towards greater failure in babies who had not received antenatal steroids ( $p=0.02$ ).<sup>17</sup>

Outcomes in two groups of preterm infants with a birth weight of 1000-1499 g were compared retrospectively over a 5-year period before (period I;  $n=57$ ) and after (period II;  $n=59$ ) the introduction of a primarily nasal CPAP-based approach to respiratory support. From period I to period II, there was a decline in the number of infants ventilated (65 versus 14%, respectively) and receiving surfactant (40 versus 12%, respectively) and in the median days of ventilation (6 versus 2, respectively) and oxygen (4 versus 2, respectively).

## CONCLUSION

Early nasal CPAP is useful in mild and moderate grade HMD. It may not be a replacement for assisted respiratory support (ventilation) in severe HMD. This study suggests that a trial of early nasal CPAP at birth is not detrimental and may be justified in case of RDS, provided early Surfactant rescue is given if the infant needs to be intubated and ventilated. Early use of CPAP will be a low cost, simple and non-invasive option for a country like India, where most places cannot provide invasive ventilation and surfactant.

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