Original Article

Effect of early nasal continuous positive airway pressure in preterm neonates with mild-to-moderate hyaline membrane disease in a rural area – An analytic prospective observational study

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ABSTRACT

Background: Respiratory distress syndrome (RDS) is the major cause of morbidity and mortality in preterm newborns. Continuous positive airway pressure (CPAP) acts by preventing atelectasis and improves functional residual capacity and arterial oxygenation. **Aims:** This study aims to evaluate the effectiveness of early nasal bubble CPAP in treating preterm neonates with mild-to-moderate RDS in the rural setting. **Materials and Methods:** It is a prospective analytic observational study done at a tertiary hospital in the rural area of southern India from December 2018 to December 2019. All babies between 28 and 34 weeks of gestation with mild and moderate RDS were included in the study. Babies with severe RDS requiring surfactant were excluded from the study. **Results:** Incidence of RDS among babies born between 28 and 34 weeks of gestation was 3.2%. Out of total 50 babies who were managed with early nasal CPAP, it proved effective in 43 babies (86%), while remaining 7 babies (14%) had to be intubated and required ventilation. Babies were studied based on radiological appearance and we found a success rate of 93.1% in moderate grade hyaline membrane disease (HMD) ($p<0.005$). **Conclusion:** Bubble CPAP is effective in treating mild and moderate cases of RDS at peripheral center and help decrease the burden at tertiary care center.

Key words: Continuous positive airway pressure, Preterm, Respiratory distress syndrome

Neonatal respiratory distress syndrome (RDS), formerly known as hyaline membrane disease (HMD), is a common complication of prematurity [1]. In babies born at 28–32 weeks, RDS occurs in up to 50% of live births [2]. In the 1960s, mechanical intermittent positive pressure ventilation was widely accepted as the standard treatment of RDS in the newborns [3]. Later in 1976, Wung *et al*. stated introduction of continuous distending pressure (CDP) as a major breakthrough and an important modality of treatment in RDS [4]. The effect of grunting respiration on arterial oxygenation also suggested that continuous positive airway pressure (CPAP) might be useful. Therefore, CPAP was considered as a missing link between the oxygen and ventilator therapy.

In high-income countries, CPAP has reduced the requirement and duration of mechanical ventilation in neonates, along with a gain in popularity as an initial method of respiratory support for premature infants [5-7]. However, mechanical ventilation is complex, requires more expertise, and is an expensive modality. Whereas, bubble CPAP is a simpler intervention for respiratory distress, economical, and more accessible in low- and middle-income countries [1,8]. With the advent of antenatal glucocorticoids inducing surfactant maturation, a decrease in the need of exogenous surfactant therapy is noted [9]. With the above background, there is a global trend favoring noninvasive ventilation and highlighting early CPAP as a primary mode of treatment even in low-income countries. There is a paucity of literature with only few studies addressing the research question [1,8,10,11]. Moreover, the available literature comprises studies done before 2015. The present study was a hospital-based study in rural India and aimed at managing babies with hyaline membrane disease with a non-invasive approach in the form of timely nasal CPAP.

MATERIALS AND METHODS

The study was conducted at a tertiary center in South India. It was a prospective analytic observational study with an aim to evaluate the effectiveness of timely nasal bubble CPAP in rural setting. The

Access this article online	
Received - 09 June 2020 Initial Review - 18 June 2020 Accepted - 28 July 2020	Quick Response code
DOI: 10.32677/IJCH.2020.v07.i08.002	

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study duration was 13 months, from December 2018 to December 2019. The study population included neonates between 28 and 34 weeks gestational age presenting with mild-to-moderate HMD. Written and informed consent was obtained from parents/guardians. We excluded neonates with congenital malformations, babies born to mothers who had received general anesthesia, phenobarbitone, pethidine, and other drugs likely to depress the baby and severe RDS cases with Grades 3 and 4 radiographic changes.

Babies were classified as mild, moderate, and severe grade HMD based on radiological findings of the X-ray [12]. All babies with HMD were evaluated clinically and monitored using Silverman Anderson (SA) scoring, and pulse oximetry. Babies with SA score of >4 or requiring fraction of inspired oxygen (FiO_2) 0.6 to maintain partial pressure of oxygen in arterial blood (PaO_2) above 60 mmHg were treated with nasal CPAP. Nose mask type of nasal interfaces was used to deliver bubble CPAP. Effectiveness of the intervention was assessed using SA score and pulse oximetry monitoring. Arterial blood gas (ABG) was performed when required, based on the unit protocol. CPAP therapy was considered successful when the baby could maintain saturation >85% without any signs of respiratory distress and with a PaO_2 >60 mmHg, partial pressure of carbon dioxide in arterial blood ($PaCO_2$) <45 mmHg, and pH between 7.35 and 7.45 with FiO_2 <0.6. Failure of CPAP was considered when there was worsening distress (SA score> 6), or recurrent apnea or increased FiO_2 requirement (>0.6) with a PO_2 <60 mmHg or PCO_2 >60 mmHg. When CPAP therapy failed, babies were ventilated and referred to a tertiary care center after surfactant administration.

Data were collected in a pro forma designed for the study and analyzed using SAS 9.4 software. "p"<0.05 was accepted as indicating statistical significance.

RESULTS

Flow diagram of the study population is depicted in Fig. 1. Incidence of preterm delivery and RDS was 12.42% and 3.2%, respectively. There were 50 neonates between 28 and 34 weeks of gestation with mild-to-moderate HMD satisfying the inclusion criteria during the study period. Out of 50 babies who were enrolled, CPAP proved to be effective in 43 babies (86%), while the remaining 7 babies (14%) required intubation and upgradation of respiratory support.

Baseline characteristics of the study population with outcome-based analysis are depicted in Table 1. As the gestational age of the baby advances, the outcome was better with 100% success rate observed in babies >33 weeks of gestation. There was statistically significant difference between success and failure groups with respect to gestational age (p<0.001).

Table 2 summarizes effect of nasal CPAP on SA score before and 6 h after initiation of therapy. It is found that success rate was 96.42% in babies of mothers who had received antenatal steroids, whereas only 72.72% of the babies improved whose mothers did not receive antenatal steroids (p<0.05). Hence, antenatal steroids

Table 1: Baseline characteristics with outcome-based analysis of the study population

Characteristics	CPAP success (n=43)	CPAP failure (n=7)	p-value
Gender			
Male	27	3	>0.05
Female	16	4	
Gestational age (weeks)			
28–30	4	6	<0.05
31–32	29	1	
33–34	10	0	
Birth weight (g)			
<1000 g	2	1	>0.05
1000–1500 g	30	6	
1501–2000 g	11	0	
Antenatal steroid status			
Received	27	1	<0.05
Not received	16	6	

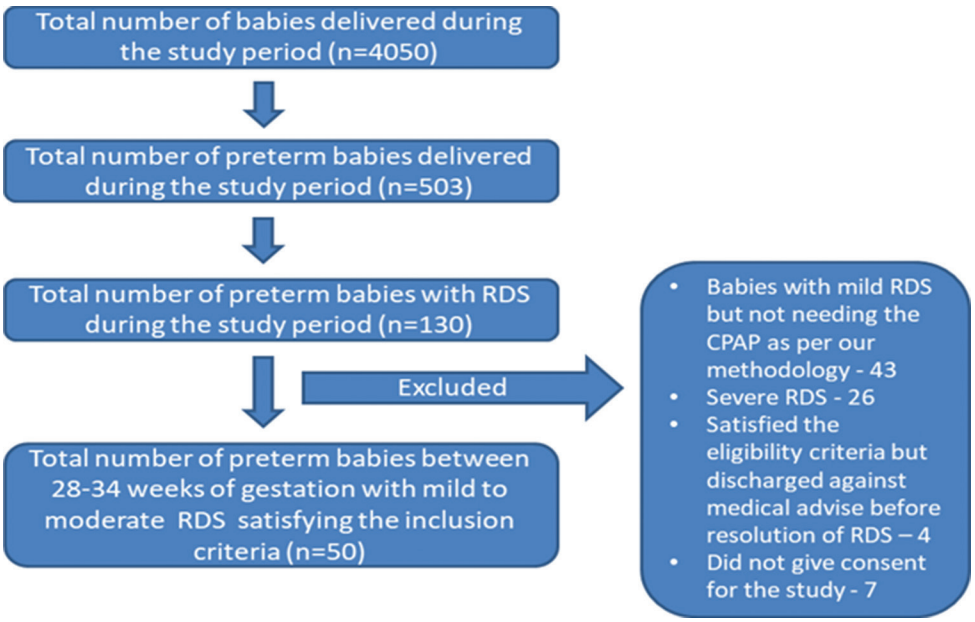

Figure 1: Flow diagram of the study population

Table 2: Distribution of SA score in the study group before and after 6 h initiation of treatment

Group	SA score before initiation of CPAP	SA score after 6 h of CPAP therapy				
		2	3	4	5	≥6
CPAP failure (n=7)	>5	0	0	1	4	2
CPAP success (n=43)	≥5	12	17	10	4	0
Total (n=50)	≥5	12	17	11	8	2

χ^2=24.50; df = 8; p<0.005

administration in mother had definitive role in better outcome of HMD.

DISCUSSION

The incidence of prematurity and HMD in our study was 12.42% and 3.2%, respectively. The incidence of HMD in this study was 3.2%. Surfactant therapy is a cornerstone in the management of severe RDS. As surfactant storage, administration, technique of asepsis, and shortage of skilled personnel are the challenges faced in rural India, we excluded severe RDS cases which required surfactant immediately after birth and focused on the mild-to-moderate cases. This was also supported by literature from an Indian study by Koti *et al*. [13], where infants with Grades 3 and 4 chest X-ray findings, and those with higher FiO2 requirement had high risk of CPAP failure needing mechanical ventilation.

Out of 50 babies who were treated with early nasal CPAP, 64% were male and 36% were female. The evidence of a poorer prognosis in boys has been widely reported in the literature [14]; however, no such finding was observed in our study. Urs *et al*. [15] also found no statistically significant difference in outcome between males and females.

We studied the relationship between gestational age of the baby at birth and the outcome. Analysis of our study results showed that outcome was better with increase in gestational age (p<0.05). Urs *et al*. [15] found better outcome in babies with gestational age of 32–34 weeks (p<0.001). Ammari *et al*. [16] demonstrated that CPAP was successful in 87.4% of infants who were ≥26 weeks of gestation.

We looked into the effect of birth weight of the babies and overall outcomes. CPAP intervention was successful in all the babies >1500 g. In babies <1000 g, 66.6% had successful results. A study by Narendran *et al*. [5] has also shown better outcomes in extremely low birth weight babies. Another study by Joris *et al*. [17] has shown significant reduction in intubation rate in babies <1500 g (from 72.1% to 30.8%; p<0.01). In our study, we did not find any significant difference in the outcome of babies based on birth weight statistically. Urs *et al*. [15] showed better outcomes with statistical significance in babies with birth weight 1000–1500 g (p<0.001).

In our study, effectiveness of early nasal CPAP was judged based on SA scoring. We found statistically significant improvement (p<0.005) in SA score after application of nasal CPAP. SA scoring also helped us to predict which babies would require upgradation of respiratory support. Similarly, Urs *et al*. showed significant improvement in Downes score after application of bubble CPAP. In a study by Pieper *et al*. [18], infants who received CPAP in circumstances, where tertiary NICU access was denied, had a significantly improved short-term survival (at 24 h), with trend toward improved long-term survival.

Boo *et al*. [19] in a study determined the predictors associated with failure of nasal CPAP in the treatment of RDS. These were moderate or severe RDS and pneumothorax during CPAP therapy. In our study, all the babies who failed CPAP had moderate RDS and no baby developed pneumothorax. Among the seven cases failing CPAP therapy, three cases had patent ductus arteriosus (PDA), three cases developed sepsis, and in one case, mother did not receive antenatal steroids. We also analyzed the role of antenatal steroid use on overall outcome of babies treated with CPAP. We found that 27 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 16 improved (p<0.05). Antenatal steroid administration helps us to predict the severity of HMD and need for invasive respiratory support. A study by Sandri *et al*. [14] showed trend toward greater failure in babies who had not received antenatal steroids (p=0.02). Urs *et al*. showed that CPAP is more effective in babies of mothers who have received antenatal steroids.

In our study, CPAP alone was effective in treating 43/50 babies (86%) with mild-to-moderate RDS. In the study by Urs *et al.*, CPAP proved to be effective in 80% of cases with HMD [15]. In a retrospective study by Ammari *et al.* [16], which analyzed 261 neonates with birth weight ≤ 1250 g, success rate of bubble CPAP was 76% in babies' ≤1250 g and 50% in babies ≤750 g. Another study by Nair *et al*. [20] showed failure rate of 10.7% in newborns with respiratory disease. Kamper *et al*. [21] results showed that the treatment was effective in 72% of infants with a birth weight ≤1500 g and in 88% of infants with a birth weight >1500 g. All above studies showed more or less similar results highlighting the efficiency of CPAP in management of preterm neonates with RDS.

Our study had a few limitations. It was a single-center study lacking generalizability. Although known statements, applying to rural settings is a great strength needed particularly in developing countries like India.

CONCLUSION

Establishment of early nasal CPAP in rural health centers is useful in treating mild and moderate cases of HMD. This is crucial as it decreases the burden in tertiary care hospitals promising effective outcomes in the babies. Use of early nasal CPAP is simple, non-invasive, and has low capital outlay.

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Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Thirupathi RK, Rani TR, Pandala P, Rakesh K, Konda KC, Singh H. Effect of early nasal continuous positive airway pressure in preterm neonates with mild-to-moderate hyaline membrane disease in a rural area – An analytic prospective observational study. Indian J Child Health. 2020; 7(8):328-331.