

EARLY VERSUS LATE INITIATION OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE FOR TREATMENT OF RESPIRATORY DISTRESS SYNDROME IN PREMATURE NEWBORNS: A RANDOMIZED CONTROL TRAIL

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ABSTRACT

Background: Respiratory distress syndrome (RDS) is an important cause of mortality and morbidity in premature infants, primarily due to surfactant deficiency. Controversies still exist in the management of RDS. Studies documenting the outcome of early CPAP therapy are very scarce in India.

Aims and Objectives: This prospective study was performed to compare the efficacy of early CPAP with late CPAP therapy in treatment of RDS in preterm infants between 28-32 weeks of gestation.

To assess the requirement of surfactant or mechanical ventilation in the 2 groups and various adverse outcomes in neonates undergoing CPAP therapy.

Materials and Methods: Fifty four preterm neonates between 28-32 weeks were studied. They were randomized into two groups of 27 each (group 1 and group 2). In group 1, newborns were given continuous distending pressure of 6cmH₂O immediately in our NICU. In group 2 newborns were put on CPAP after development of respiratory distress, scoring was based on Silverman- Andersen score, Newborns with score of >3 were included in the study.

Results: Among 54 preterm neonates, Mean gestational age and weight at the time of admission were comparable between two groups (early vs. late: 30.7±0.95 vs. 30.57±1.01 weeks, birth weight 1065.2±82.2 vs. 1059.8±86.8 gm). The need for MV and surfactant was also less in early CPAP group (MV: 19% vs. 48%, P<0.05, surfactant: 15% vs. 45%, P<0.05). The mean hospital stay was significantly less in the early CPAP group, 29.96±6.7 days compared to 33.8±6.8 days in late group with significant P value of 0.01. Mortality was also high in late CPAP (11%) compared to early (4%) group though the p value was not statistically significant.

Conclusion: Early CPAP is more effective than late CPAP group for the treatment of RDS. In addition, early use of CPAP would reduce the duration of hospital stay, need for invasive procedures such as mechanical ventilation and surfactant administration. These results may be particularly relevant for resource limited setting.

Keywords: *Continuous Positive Airway Pressure, Premature Infant, Respiratory Distress Syndrome, Surfactant, Mechanical Ventilation*

INTRODUCTION

Respiratory distress syndrome (RDS) is an important cause of mortality and morbidity in premature infants, primarily due to surfactant deficiency (Sinha *et al.*, 2008). Assuming the incidence of RDS to be 1.2% among live births, nearly 1, 86,000 infants are affected in India with RDS (NNF India 2002-2003). With the reported mortality of 57% to 89% among infants with RDS, nearly 100,000 infants each year are estimated to die due to RDS (Kumar *et al.*, 1996). Lower the gestation higher is the incidence of RDS, accounting for nearly 80% incidence in preterm infants less than 28 weeks.

For two decades, the standard treatment for very preterm infants was with assisted ventilation and surfactant. In an attempt to prevent the injuries caused by mechanical ventilation, there has been a search for less aggressive ways of promoting respiratory support for these patients (Jobe *et al.*, 2001), it has been hypothesized that the avoidance of ventilation might lead to less morbidity and mortality.

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Nasal continuous positive airway pressure is a well-established modality for providing ventilatory support to spontaneously breathing infants. It has been used in a variety of clinical situations. nCPAP is a modality that supports spontaneous ventilation by providing a positive airway pressure throughout the whole respiratory cycle (Cheema and Ahluwalia, 2003).

A wide variety of devices are used to deliver CPAP, including variable flow driver devices, single or binasal prongs where pressure is generated by a column of water (bubble CPAP) or a ventilator. It has been suggested that use of CPAP in the poorly compliant lung may promote lung volume recruitment and augment the efficiency of gas mixing. CPAP delivered by underwater seal causes vibration of the chest due to gas flow under water; and these vibrations simulate waveforms produced by high frequency ventilation (Van Marter *et al.*, 2000).

CPAP, when applied to premature infants with RDS, re-expands collapsed alveoli, splints the airway, reduces work of breathing and improves the pattern and regularity of respiration (Carlos, 2006).

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 settings like India. Even though early CPAP therapy has been shown to be successful in some clinical trials in the management of RDS, studies documenting its efficacy are very scarce in India.

With this background present study is conducted to assess the efficacy of early versus late use of CPAP in treatment of RDS in preterm babies born between 28-32 weeks of gestation.

MATERIALS AND METHODS

Inclusion Criteria:

1. Preterm babies born between 28- 32 weeks who are appropriate for gestational age.
2. Babies requiring minimal resuscitation at birth.

Exclusion Criteria:

1. Babies with congenital anomalies like, cleft lip & palate, congenital diaphragmatic hernia, choanal atresia, major cardiac anomalies etc
2. Babies requiring advanced resuscitation at birth.
3. If CPAP is instituted for other indications like Apnoea.
4. H/o maternal infection compromising respiratory system.

It was a hospital based randomized controlled study conducted at neonatal intensive care unit of MVJ MC & RH between November 2016 to August 2018. It was approved by the institutional Ethical Committee. After taking an informed consent from the parent / legal guardian. Inborn neonates with gestational age between 28 to 32 weeks requiring minimal resuscitative efforts and satisfying inclusion criteria were enrolled.

In early CPAP group i, e Group 1 newborns were put on CPAP before the onset of respiratory distress, respiratory distress scoring was based on Silverman Andersons Score (SAS). Score of <3 were included in this group.

In late CPAP group i, e Group 2 newborns were put on CPAP after the onset of respiratory distress. Newborns with SAS score of >3 were included in this group.

In both groups continuous distending pressure was given using Fisher Paykel bubble CPAP. PEEP was started at 5cm of H₂O and was adjusted to minimize the chest retractions. FiO₂ was adjusted to maintain SpO₂ 88% to 92%. Vital parameters were monitored continuously.

Bubble CPAP was considered to be successful if the respiratory distress improved and the baby could be successfully weaned off from CPAP. The criteria for weaning was absence of respiratory distress (minimal or no retractions and respiratory rate between 30 and 60 per minute) and SpO₂>90% on FiO₂ <30% and PEEP <5 cm of water. Infants were diagnosed to have failed CPAP and were started on mechanical ventilation when they, Had >12 episodes of apnea, pCO₂>65mmhg, requirement of FiO₂ of

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>0.4 to maintain SpO₂ of 88% to 92%. Surfactant administration was considered if on CPAP and FiO₂ >0.4, or on MV and FiO₂ ≥0.35.

Primary outcome was to assess the need for mechanical ventilation and surfactant (Neosurf at 5mk/kg was administered when required). Secondary outcome was to assess the complications like BPD by supplemental oxygen usage at 36weeks postmenstrual age, PDA by clinical diagnosis, IVH based on ultrasonographic examination, ROP based on ophthalmic examination, positive septic screen based on CRP or Blood culture and mortality among both groups. Duration of hospital stay among both the groups was studied.

Statistical Analysis:

The data collected was entered systematically in Microsoft Excel. Tables and charts generated using MS Excel and MS Word. Statistical analysis was done by taking the means of quantitative variables between the two independent groups using unpaired-t test. Association between 2 or more qualitative and categorical variables was assessed using the chi-square test. Test, p value < 0.05 was considered statistically significant.

RESULTS

Fifty four neonates were included in the study, twenty seven in each group. The demographic data of the neonates are shown in Table 1

Table 1: Base line Demographic data of the study population

Characteristics	Early n CPAP (n=27)	Late n CPAP (n=27)	p value
Gestational Age(in weeks)	30.78±0.95	30.572±1.01	0.46
Birth Weight (in grams)	1065.2±82.2	1059.8±86.8	0.82
Male Sex (%)	62%	56%	0.2
Antenatal Steroid use(%)	63%	56%	0.5
Mode of Delivery			
Cesarean %	70%	63%	0.5
Vaginal Delivery(%)	30%	37%	0.5

There was no significant difference between the two groups with regard to baseline demographic data like, Gestational age, birth weight, sex, antenatal steroid use and mode of delivery. Hence the groups were comparable.

Table 2 shows the primary outcome of the study, the need for mechanical ventilation and surfactant.

Table: 2 Primary outcomes of the Study.

Characteristics	Early group (n=27)	Late group (n=27)	P value
Need for Mechanical Ventilation	5(19)	13(48)	0.03
Need for Surfactant	4(15)	12(45)	0.03

Table 3: Secondary outcomes of the study

Characteristics	Early group (n=27)	Late group (n=27)	p Value
BPD	1(4)	3(11)	0.3
VAP	0	4(15)	0.05
CPAP Belly	2(7)	3(11)	0.4
Nasal septal perforation	nil	nil	-
Air leaks	nil	nil	-
ROP	1(4)	4(15)	0.1
PDA	4(15)	7(26)	0.2
IVH	2(7)	3(11)	0.4
Sepsis	7(26)	11(41)	0.01
Hospital Stay	29.96±6.7	33.8±6.8	0.01
Mortality	1(4)	3(11)	0.3

DISCUSSION

Several alternatives have been proposed to minimize lung injury in preterm infants, one of them being the early application of CPAP, although there are doubts about its efficacy. The early CPAP system became a subject of study after a publication in (1987 by Avery *et al.*). had shown a significantly lower incidence of the use of oxygen in newborns at 28 days at Columbia University compared to major American hospitals. The initial hypothesis of the present study was that, with early application of distention pressure, alveolar collapse would be reduced, with a consequent lower consumption of surfactant and a less frequent need for mechanical ventilation.

The baseline demographic data which is presented in table 1 in means of gestational age, birth weight, sex, antenatal steroid use, and mode of delivery were comparable between the groups.

As shown in Table 2 the need for mechanical ventilation was lesser in the early CPAP group 19% compared to 48% in late group with significant p value of 0.03. In the study conducted by Morely et al 37% of prophylactic and 51% of curative group required mechanical ventilation..

The need for surfactant was higher in late CPAP group 45% compared to 15% in early group with significant difference of P=0.03. Morely et, al study also showed that need for surfactant was less in prophylactic group 9%, compared to 21% in curative group. In the study conducted by Zohreh et al, need for surfactant was 38.9% in prophylactic CPAP group and 63% in curative CPAP group, this might be probably because they included lesser weight babies.

Associated morbidities of preterm neonates like ROP, IVH, and PDA were more in late group compared to the early group, though the values (table 3) were not statistically significant.

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Early CPAP group spent lesser duration on CPAP and Mechanical Ventilation compared to late group, so complications like BPD and VAP were higher in late group compared to early CPAP group. Morely et al did not find any significant differences in BPD and death between groups.

Incidence of sepsis diagnosed based on CRP and Blood culture was also higher in late (41%) CPAP group compared to early (26%) with significant p value of 0.01. The total duration of hospital stay was less in the early (29.96±6.7) CPAP group compared to the late group (33.8±6.8) with p value 0f 0.01.

Overall the mortality was higher in late (11%) CPAP group compared to the early (4%) group though the values were not statistically significant. In the study conducted by Zohreh *et al.*, (2013) there was 16.7% and 22.7% mortality in early and late CPAP group respectively.

Establishing a NICU with mechanical ventilation would require high level of expertise and trained personnel, which is far from reality in many of the peripheral and district hospitals in developing countries. In our study, surfactant administration was reduced in the early CPAP group. Therefore we found that early use of CPAP could be cost effective in the treatment of RDS.

Conclusion

Early use of CPAP is an effective and safe method for the treatment of RDS in preterm newborns. Moreover, early CPAP could reduce the need for some invasive procedures such as intubation and mechanical ventilation

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