Original article

Noninvasive respiratory support in the preterm neonate with hyaline membrane disease: Bubble CPAP *vs* Conventional CPAP - A randomised controlled trial

Eribaweimon Shilla*, Leslie Lewis
Email: eribain@yahoo.co.in

Abstract

Background: Continuous Positive Airway Pressure (CPAP) is a noninvasive, gentle method of providing respiratory support to spontaneously breathing neonates. **Objective:** To compare the effectiveness of bubble CPAP (B-CPAP) over conventional CPAP (C-CPAP) in view of improvement in the severity of respiratory distress in preterm neonates with hyaline membrane disease (HMD). **Methods:** The targeted populations were all preterm and late preterm neonates admitted in neonatal intensive care unit (NICU) with HMD and respiratory distress, requiring noninvasive ventilation. Neonates who met the inclusion criteria were randomly allocated to either B-CPAP or C-CPAP using random table method. CPAP was started at the earliest signs of respiratory distress and postextubation. **Result:** Respiratory distress was assessed before and after initiation of CPAP based on Downe's score. The decrease in Downes score was statistically significant in the B-CPAP group compared to C-CPAP group. Primary CPAP failure was 23% (7/30) in the B-CPAP group compared to 10% in the C-CPAP group (3/30) ($p = 0.16$). The number of days on CPAP, oxygen therapy and NICU stay showed no significant difference. Complications of CPAP were not significantly different. **Conclusions:** B-CPAP is as effective as C-CPAP in improving respiratory distress. However, CPAP failure rates are higher in B-CPAP group with preterm of extreme low birth weight babies (<1000 g). B-CPAP is one of the most effective and economical mode of noninvasive respiratory support for preterm neonates with HMD.

Keywords: Neonates, Hyaline membrane disease, Mechanical Ventilation, Continuous positive airway pressure.

Introduction

Continuous positive airway pressure (CPAP) is a noninvasive and gentle method of providing respiratory support to spontaneously breathing neonates. The pressure applied is continuous, during both inspiration and expiration. CPAP is used to maintain lung expansion under conditions that cause alveoli and small airways to collapse or fill with fluid.[1] Constant application of positive pressure helps to open up the alveoli and increase the functional residual capacity (FRC) of the lung resulting in better gas exchange as recruitment takes place.

The effect of CPAP is mainly seen in newborn with respiratory distress syndrome (RDS) or hyaline membrane disease (HMD). CPAP increases the FRC above the closing volume so that the terminal airway remains open throughout the respiratory cycle. Endogenous surfactant production reduces the surface tension, thereby preventing the collapse of the alveoli.

Eribaweimon Shilla, MSc RT, CRT
Assistant Professor, Department of Respiratory Therapy, Manipal College of Allied Health Sciences, Manipal, India

Leslie Lewis, MBBS, DCH, DNB
Professor of Paediatrics and Head, Neonatal Intensive Care Unit, Kasturba Medical College, Manipal

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Physiologically, CPAP results in better oxygenation, carbon dioxide (CO_2) removal and improves blood pH. CPAP splints the upper airway and prevents obstruction and apnoea.[2] The J-receptors are stimulated by the stretch of the lung pleura and provide positive feedback to the respiratory centres by Hering Breuer reflex.

Based on the physiological principles there is a strong evidence for the use of early CPAP as a primary modality, with or without surfactant for newborns with RDS/HMD. CPAP could be used postextubation to prevent atelectasis, apnoea and reintubation. In the delivery room, CPAP may be prophylactically used in preterm infants.

Both conventional and bubble CPAP are clinically effective if applied early in the post extubation period. The use of B-CPAP in infants has been shown to significantly reduce minute ventilation and respiratory rate with no change in transcutaneous carbon dioxide or oxygen saturation, compared with mechanical ventilator CPAP or C-CPAP.[3]

This study was designed to compare the effectiveness of bubble CPAP (B-CPAP) over conventional CPAP (C-CPAP) in reducing the severity of respiratory distress in preterm neonates with respiratory distress syndrome (RDS) or hyaline membrane disease (HMD). It also aimed to study the duration of CPAP, oxygen therapy requirement, ICU stay and immediate complications of B-CPAP over C-CPAP.

Patients and methods

This was a prospective, randomised control study conducted at Neonatal Intensive Care Unit (NICU), Kasturba Hospital, Manipal. The study period was from 1st February 2010 to 31st January 2011. All preterm and late preterm neonates who were admitted in NICU with HMD /RDS having respiratory distress and requiring noninvasive ventilation were included in the study based on the inclusion and exclusion criteria.

Inclusion criteria were preterm and late preterm neonates diagnosed to have RDS/HMD and those who were extubated from invasive mechanical ventilation. Preterm neonates with congenital malformations were excluded.

Neonates who met the inclusion criteria were randomly allocated to either B-CPAP or C-CPAP group using random table method. CPAP was started at the earliest sign of respiratory distress (tachypnea, retraction, cyanosis, air entry and grunting) by using Downes' scoring system. A Downe's score of >2 indicated that patient is in respiratory distress and CPAP is indicated. A score of >6 required intubation and mechanical ventilation. The other parameters that were documented were heart rate, saturation, temperature and blood pressure.

The study protocol was approved by the Institutional Ethics Committee. Information regarding the treatment and participation of the newborn in the study was explained and consent was taken from the parents.

The two types of CPAP used were as follows:

B-CPAP: The Fisher & Paykel™ healthcare equipment components were attached and fitted on a stand *(Figure 1)*. The circuit had an inspiratory and expiratory limb. The inspiratory limb ensured gas flow from blender to the humidifier and then to the patient. Active humidification was provided to prevent nasal dryness and mucocilliary dysfunction. The expiratory limb was connected to the bubble chamber filled with distilled water to the required level. The depth to which the expiratory limb was inserted determined the level of CPAP. The bubbling that occurred during the respiratory cycle was conducted back to the chest and caused a '*wiggling*'. This oscillation was said to improve gas exchange and FRC.

Figure 1: Complete set up of bubble CPAP

C-CPAP: The Dräger Babylog machine was connected to the air and oxygen gas inlet *(Figure 2)*. The circuit had an inspiratory and expiratory limb. The inspiratory limb ensured gas flow from the machine to the humidifier and then to the patient. The heated wire in the inspiratory limb maintained the humidified gas till it reached the patient. The expiratory limb was connected to the exhalation port of the ventilator, which had a solenoid diaphragmatic valve to control CPAP.

CPAP pressure was increased or decreased by increasing or decreasing the depth of immersion of expiratory limb into the bubble chamber in B-CPAP or turning the knob of CPAP pressure in C-CPAP. CPAP was commenced with a pressure of 5 cm H_2O and adjusted according to the chest retraction, with the set flow rate of 5-8 litres per minute to produce a continuous flow. In some patients where blender was not connected, air and oxygen flow rate were adjusted to get a desired FiO_2 and confirmed by an oxygen analyser. FiO_2 was first set at room air (0.21) and if oxygen saturation dropped below 88%, oxygen was increased gradually.

Figure 2: Complete set up of C-CPAP

The parameters monitored for assessing adequacy and complications of CPAP were heart rate, temperature, respiratory rate, blood pressure, SpO_2 and abdominal distension. Oxygen saturation by pulse oximetry, heart rate, respiratory rate and blood pressure were monitored continuously using monitor.

Statistical analysis was done with statistics software SPSS 16, SPSS, Chicago, Illinois. Continuous measures between groups were compared using Student's t-test. Nonparametric continuous outcomes were compared using Wilcoxon signed ranks test and Mann Whitney *U* test. Chi-square test was done for categorical variables. P value of <0.05 was considered statistically significant.

Results

A total of 60 preterm newborns presented with HMD/RDS and respiratory distress who were admitted in NICU during the period of 1st February 2010 to 31st January 2011 were enrolled into the study *(Figure 3)*.

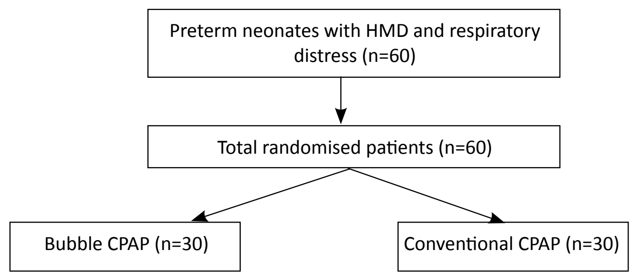

Figure 3: Consort statement of the study

The mean gestation age and gender did not differ between the two groups. However, the newborns with extreme low birth weight (< 1000 g) were more in the B-CPAP group *(Table 1)*.

Table 1: Baseline characteristics of the infant at the time of initiation of CPAP

Base line characteristic	B-CPAP (n=30)	C-CPAP (n=30)
Gestational age in weeks (mean ± SD)	31.6 ± 2.9	31.5 ± 2.0
Male: Female	20:10	21:9
Weight in g (mean ± SD)	1491 ± 607.5	1485 ± 332.8
< 1000 g (n)	9	0
1001-1500 g (n)	8	17
1501-2000 g (n)	6	11
> 2001 g (n)	6	2

Respiratory distress was assessed before and after initiation of CPAP based on Downes' score. The neonates in B-CPAP group had a median Downes' score of 4 and it reduced to 1 with intervention whereas the neonates in C-CPAP group had a median Downes' score of 3 which reduced to 1 with intervention. The decrease in Downes' score was statistically significant in the B-CPAP group compared to C-CPAP group *(Table 2)*.

Table 2: Severity of respiratory distress at baseline and change with intervention

Types of CPAP		Severity of respiratory distress (Downes' score)	
		Median	Interquartile range
C-CPAP	Baseline	3	2 - 4
	After intervention	1	
B-CPAP	Baseline	4	2 - 5
	After intervention	1	

Wilcoxon Signed ranked test p < 0.05

The number of days on CPAP, oxygen therapy and NICU stay were also not different between the two groups *(Table 3)*.

Table 3: Outcome measures of duration of CPAP, oxygen therapy and NICU stay.

		No. of days on CPAP*	No. of days on O_2 therapy*	No. of days in NICU*
C-CPAP	Median	2	0	25
	Range	1 - 10	0 - 6	6 - 58
	Interquartile range	2 - 4	0 - 1	10.8 - 42.3
B-CPAP	Median	2	0	20
	Range	1 - 10	0 - 7	2 - 93
	Interquartile range	2 - 5	0 - 2	10 - 33.8

Mann-Whitney *U* test *p > 0.05

Neonates with CPAP failure requiring intubation in C-CPAP group was 10% (3/30) and in B-CPAP was 23% (7/30) but this did not reach statistical significance (p = 0.16). The number of extremely low birth weight neonates (<1000 g) were more in B-CPAP and this may be the reason for higher incidence rate of intubation in the B-CPAP group.

Complications of CPAP such as both abdominal distension and nasal septum damage were assessed in both groups and were found to be statistically not different *(Table 4)*.

Table 4: Incidence of CPAP failure in both the groups

	B-CPAP		C-CPAP		P value
CPAP Failure	No	Yes	No	Yes	0.16
	23 (76%)	7 (23%)	27 (90%)	3 (10%)	

Chi Square test

Table 5: Complications of CPAP in both the groups

Complication	B-CPAP		C-CPAP		P value
	No	Yes	No	Yes	
Abdominal distension	28 (93%)	2 (7%)	22 (73%)	8 (26%)	0.08
Nasal septum damage	25 (83%)	5 (7%)	23 (77%)	7 (23%)	0.51

Chi Square test

Discussion

Respiratory distress syndrome (RDS) is the leading cause of morbidity and mortality in the premature neonatal population. Therefore it is crucial to find the most effective and efficient techniques to treat this population suffering from RDS. Bubble CPAP has often been employed as a safe, efficient and effective way of applying noninvasive ventilation. It is used to avoid the need for intubation and mechanical ventilation thereby reducing lung injury and other morbidities as well as decreasing hospital stay.

In this study the basic outcome was analysis of respiratory distress before and after CPAP based on Downes' score. Both B-CPAP and C-CPAP reduced the Downes' score to 1. However, nine of the neonates in B-CPAP group were of very low birth weight and had a median Downes' score of 4 at baseline as compared to 3 in the C-CPAP group. Whether C-CPAP also would have had similar results in those very low birth weight infants is not clear. Prashant *et al*, is their study found that there was statistically significant improvement in Downes' score after application of B-CPAP.[4] The success rate of their study was seen because newborns with RDS were initiated early to B-CPAP at a Downes' score of 4.

The study done by Sandri *et al*[5] have shown higher need for respiratory assistance in male infants with RDS. In this study also, the number of males were higher than females. In the study by Boo *et al*, moderate RDS was one of the predictors for failure of CPAP.[6] In our study, infants with lower birth weight < 1000 g had a higher risk for CPAP failure.

The current techniques used in noninvasive CPAP delivery vary with different settings but the role of CPAP in the management of respiratory distress is well accepted. The noninvasive method of CPAP delivery in respiratory distress is associated with reduction in the need for intubation and reintubation. This study showed that B-CPAP is as good as C-CPAP and it also proved to be more beneficial when the post respiratory distress score was assessed.

In a study done by Liptsen E *et al*, 18 preterm neonates on B-CPAP were associated with increased work of breathing (WOB) when compared to variable flow nasal CPAP.[7] According to the data of this study, it was postulated that B-CPAP will have greater failure rates. However, Lee *et al* suggested that ventilation was more effective with B-CPAP than C-CPAP.[3]

The limitation of our study is that during randomisation the subclassification of weight, gestation and reintubation was not analysed due to small sample size.

Conclusions

Bubble CPAP could be considered as one of the potential mode of noninvasive CPAP for preterm neonates with HMD. Bubble CPAP is as effective in improving the severity of respiratory distress in comparison to conventional CPAP. The number of days on noninvasive ventilation, oxygen therapy, NICU stay and complications are similar with both B-CPAP and C-CPAP.

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