ejpmr, 2021,8(4), 643-648

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

USE OF BUBBLE CONTINUOUS POSITIVE AIRWAY PRESSURE (bCPAP) FOR PREVENTION OF RESPIRATORY DISTRESS IN PRETERM INFANTS

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Article Received on 20/02/2021 **Article Revised on 10/03/2021** **Article Accepted on 30/03/2021**

ABSTRACT

Introduction: Preterm babies contribute the major share of total admission in neonatal intensive care units among the world. Many of these babies present with respiratory distress of variable degrees. Contemporary, continuous positive airway pressure (CPAP) is a popular and effective modality of management of preterm newborns. The commonest use is for respiratory distress syndrome or respiratory distress for any other cause when the baby fails to maintain oxygen saturation because of poor lung compliance. However, prophylactic use of CPAP to prevent respiratory distress in preterm babies is a relatively unexplored subject. It would be interesting to see the effect of elective CPAP in preterm babies in prevention of respiratory distress. **Objective:** This study was designed to evaluate the efficacy of Bubble CPAP or the prevention of respiratory distress in preterm infants. **Method:** This randomized trial was carried out at the Neonatal Intensive Care Unit (NICU), Department of Neonatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. A total of 116 inborn preterm (gestational age: 28-32 weeks and / birth weight: 1000-1500gms) infants were enrolled in this study. In the intervention groups, respiratory support was given in the form of Bubble CPAP prophylactically within 30 minutes of birth and in the control group; respiratory support was started considering the severity of respiratory distress as per existing institutional guidelines. If the diagnosis of RDS was made, the baby was given surfactant. Surfactant was administered by InSurE approach (Intubation, Surfactant, and Extubation to CPAP). **Result:** Prophylactic use of Bubble CPAP decrease the time to improve respiratory distress: (3.14±2.74) vs 3.58±2.12 days, p-value: >0.05); decrease incidence of RDS (40% vs 46%, p- value: > 0.05), decrease requirement of surfactant (20% vs 28%), p-value: >0.05), and decrease switch to mechanical ventilation (14% 18%, p-value: > 0.05). About 80% of both groups had received prenatal steroids. Prophylactic use of BCPAP decrease length of hospital stay (28.34±12.18vs 30.74±12.24 days), increase frequency of sepsis (22% vs 18%), decrease number of ROP (16% vs 22%). Only complications of nasal septal damage (p-value: <0.05) demonstrate statistically significance between the intervention and the control group. **Conclusion:** Prophylactic use of Bubble CPAP did not show any significant advantage for the prevention of respiratory distress in preterm infants of 28-32 weeks gestation.

KEYWORDS: Preterm Infants, Respiratory distress, Prophylactic Bubble Continuous Positive Airway Pressure, Surfactant, and Mechanical ventilation.

INTRODUCTION

Every year, an estimated 15 million babies are born preterm and this number is increasing and over one million children die each year due to complications of preterm birth.[1] Prematurity is the second leading cause of death in children under five years and the single most important cause of death in the critical first month of life.[2] The worldwide estimate of preterm birth ranges 5-18% and Bangladesh occupies 7th position among ten countries with the highest number of preterm birth across the world. The prevalence of low birth weight (LBW) in Bangladesh is 36%.[1] Respiratory distress is a frequent complication in preterm infants with high morbidity and mortality despite advanced in neonatal intensive care.[3]

Although resource-intensive, bubble continuous positive airway pressure (bCPAP) is a relatively simple, non-invasive, low cost, and effective therapy for respiratory distress and the complications and expected clinical course under a variety of circumstances are well understood. It is a simple, low-cost, and non-invasive method of ventilating a sick newborn, which could be a boon for babies born in resource- restricted countries. If it uses early and judiciously in infants with respiratory distress, CPAP can save many lives and reduce upward referrals.[4] Use of low-cost Bubble CPAP system to treat neonatal respiratory distress resulted in a 27% absolute improvement in survival.[5] Continuous positive airway pressure (CPAP), often thought to be the 'missing link' between supplementary oxygen with head-box and mechanical ventilation. It is a simple, inexpensive, and gentle mode of respiratory support in preterm low birth weight infants.[6] There is currently insufficient information to evaluate the effectiveness of prophylactic nasal CPAP in very preterm infants.[7] Cohort studies using historical controls have suggested that prophylactic nasal CPAP in very low birth weight (VLBW) infants are effective in reducing the need for IPPV without worsening other measures of neonatal outcome. CPAP and early selective InSurE approach reduced the need for mechanical ventilation and surfactant in VLBW infants without increasing morbidity and death.[8] CPAP is an alternative to intubation and surfactant in preterm infants.[9] The use of early Bubble CPAP significantly decreases delivery room intubations; use of postnatal steroids and days on mechanical ventilation.[10] Widespread use of a simple circuit to deliver Bubble CPAP system has the potential for saving lives in small hospitals where there is no facility for mechanical ventilation.[11] The device is reasonably inexpensive and is suitable for use at secondary and tertiary health institutions for the care of the preterm infant with RDS.[12] The early use of bCPAP management increased in the surviving infants over time, whereas the use of surfactant decreased and the incidence of BPD decreased from 33% to 6%.[13]

OBJECTIVE

General objective

- To compare the clinical outcome of preterm babies who received Bubble CPAP and the babies who received the conventional support

Specific objective

- To evaluate the efficacy of Bubble CPAP for the prevention of respiratory distress in preterm infants.
- To find out the respiratory outcome of preterm babies
- To identify complications of Bubble CPAP

METHODOLOGY

Study type

- It was a Randomized Controlled Trial (RCT) study

Place and period of study

Neonatal Intensive Care Unit (NICU), Department of Neonatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from 1st April 2013 to 31st July 2014 (Total 16 months).

Sample size

- Total: 116 neonates who had met the criteria.

Inclusion criteria

- Preterm infants of 28-32 weeks gestation and/ birth weight 1000-1500 gms

Exclusion criteria

- Progressive respiratory failure :PH: <7.2, PCO2) <60 mmHg, PO> :250 mmH(g with FiO2: 0.8
- Conditions with imminentmechanical ventilatory support (severe cardio-respiratory compromise, poor respiratory drive)
- Certain congenital malformations of the airway(choanal atresia, cleft palate, t-racheo iesophageal fstula, congenital diaphragmatic hernia)
- Intrauterine growth restriction (IUGR) baby and Infant of diabetic mother (IDM)

Study procedure

The study infants were enrolled according to the inclusion criteria- all infants are inborn, gestational age was 28-32 weeks (more than 27 weeks and 6 days and not more than 32 weeks and 6 days). Informed written consent was taken from parents or responsible caregiver. Infants were randomly allocated to either bCPAP or control group, eligible patients entered the trial based on a 1:1 treatment allocation to prophylactic group or control group, randomized blocks of six were used to ensure treatment balance between the two arms. A detailed history was taken from the mother or caregiver and from the obstetric records; the clinical examination was done and the findings were enrolled in the data collection sheet. Gestational age was calculated based on mothers' last menstrual period and or early pregnancy ultrasound scan or New Ballard Score (NBS). Birth weight was taken by a digital weighing scale **[SALTER, Model-914]**

Case group: Respiratory support was given in the form of Bubble CPAP (**Fisher & Paykel, Model: PM 5300, New Zealand)** prophylactically within 30 minutes of birth. Initial settings of bCPAP were FiO2: 0.5, Pressure (PEEP): 5 cm H2O, Flow: 5 L/min. **Control group:** Respiratory support was started considering severity of respiratory distress as per existing institutional guidelines. If the baby developed progressive respiratory distress on CPAP during the intervention, the baby was evaluated and managed accordingly. If the diagnosis of RDS was made (based on clinical and chest x-ray evidence), the baby was given surfactant (**Survanta, Beractant, Abbott laboratories, USA)**. It was given when required FiO2 was >0.4 on CPAP and was administered by ***InSurE*** **approach** (Intubation,

Surfactant, and Extubation to CPAP). An arterial blood sample for blood gases was taken before surfactant treatment in all cases.

Data Collection

A preformed data collection sheet including history, clinical examination, investigation results were used for data collection.

RESULTS

A total of 168 neonates were admitted to the NICU during the study period. Out of them 116 infants were enrolled under the study. They were randomly assigned to either intervention (n=58) or control (n=58) groups. Two infants in the intervention group and one in the control group did not complete the treatment. Thirteen infants (six in the intervention group, and seven in the control group) died during the study period. Thus, the clinical data of the 100 infants who completed the trial was used for analysis.

Table 1: Demographic data and clinical characteristics of 28-32 weeks infants.

Variables	Intervention (n=50)	Control (n=50)	p-value
Antenatal steroids	41 (82%)	40 (80%)	0.58
Birth-weight (g)	1293.8 ± 139.7	1272.2 ± 144.93	0.45
Gestational age (wks)	30.2 ± 1.2	30.36 ± 0.98	0.65
Male sex	31 (62%)	24 (48%)	0.67
Cesarean section	33 (66%)	30 (60%)	0.53

Numerical variables are expressed as mean ± SD. and categorical variables as numbers (%). Independent two-tailed t-test and chi-squared test were done.

Table 2: Respiratory outcome in the 28-32 weeks infants.

Variables	Intervention(n=50)	Control(n=50)	p-value
Time to improve respiratory distress (d)	3.14±2.74	3.58±2.12	0.37
Number of RDS (%)	20 (40%)	23 (46%)	0.54
Need for Surfactant (%)	10 (20%)	14 (28%)	0.34
Switch to MV (%)	7 (14%)	9 (18%)	0.58

Numerical variables are expressed as mean ± SD and categorical variables as numbers (%). Independent two-tailed t-test and chi-squared test were done

RDS: Respiratory Distress Syndrome, MV: Mechanical Ventilation.

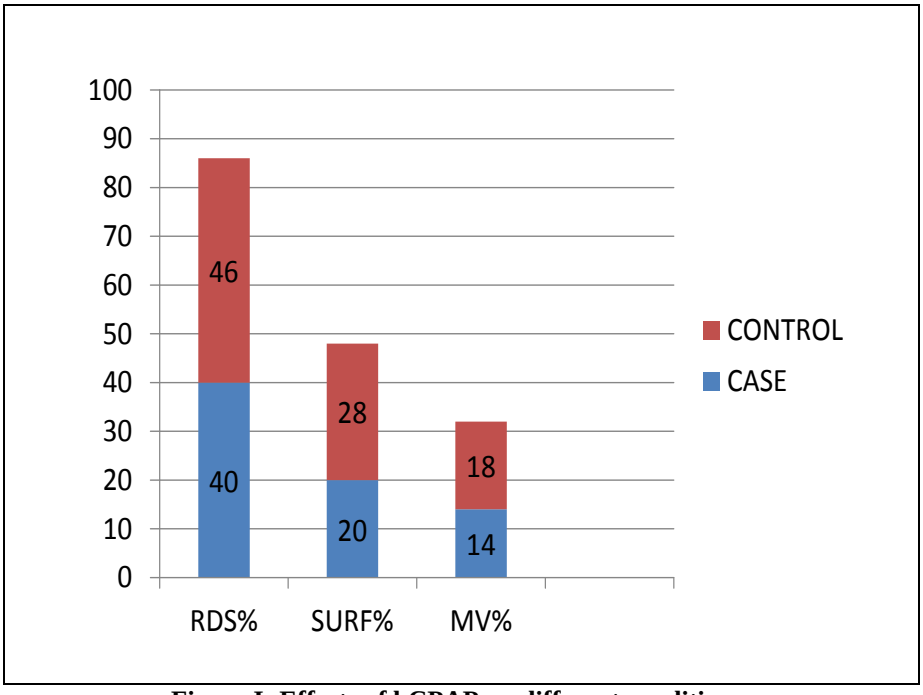

Figure I: Effects of bCPAP on different conditions.

FIGURE- I: shows the prophylactic use of bCPAP decreases the incidence of RDS (40 vs 46%), decrease the requirement of surfactant (20 vs 28%), and decreases switch to mechanical ventilation (14 vs 18%).

RDS: Respiratory Distress Syndrome, MV: Mechanical Ventilation.

Table 3: Clinical outcome in the 28-32 weeks infants.

Variables	Intervention (n=50)	Control (n=50)	p-value
Length of hospital stay (d)	28.34 ± 12.18	30.74 ± 12.24	0.32
Sepsis (%)	11 (22%)	9 (18%)	0.61
ROP (%) *	8 (16%)	11 (22%)	0.44

Numerical variables are expressed as mean ± S.D. and categorical variables as numbers (%). Independent two-tailed t-test and chi-squared test were done.
ROP: Retinopathy of prematurity*

Table 3: shows that the prophylactic use of bCPAP decreases the length of hospital stay (28.34 ± 12.18 vs 30.74 ± 12.24 days), increase the incidence of sepsis (22% vs 18%), decrease the incidence of ROP (16% vs 22%).

Table 4: Complications of BCPAP in the 28-32 weeks infants.

Variables	Intervention (n=50)	Control (n=50)	p-value
Nasal septal damage (%)	4 (8%)	0 (0%)	**0.04**
Pneumothorax (%)	2 (4%)	0 (0%)	0.15
CLD	1 (2%)	2 (4%)	0.55
CPAP belly syndrome	1 (2%)	0 (0%)	0.31

Categorical variables are expressed as numbers (%) and chi-squared test are used.
CLD: Chronic lung disease
Table 4: shows that complications (nasal septal damage, pneumothorax, CPAP belly syndrome) were seen only in the intervention group. Only septal damage **(p-value: < 0.05)** showed statistical significance.

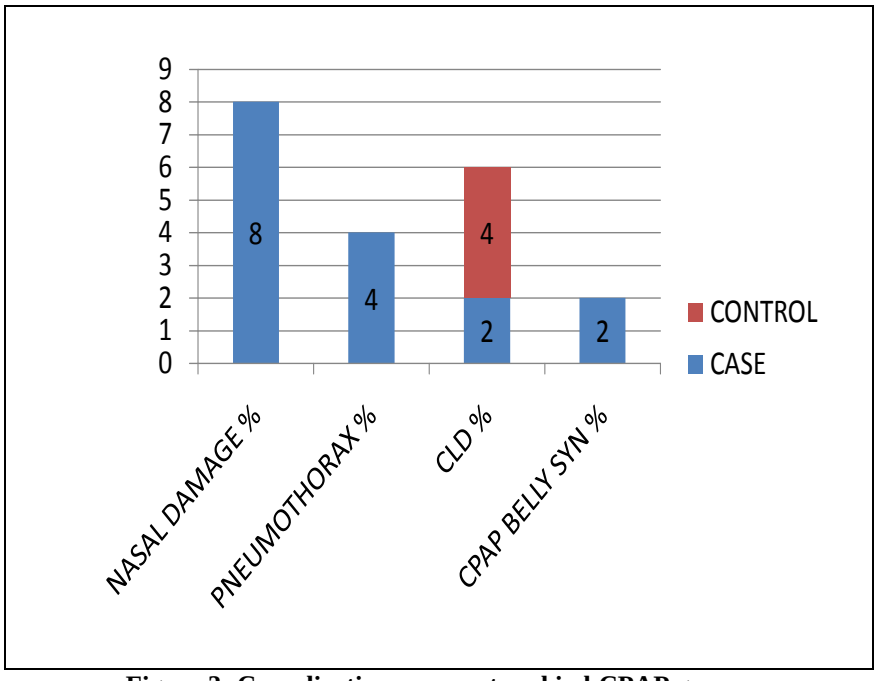

Figure 3: Complications encountered in bCPAP group.

FIGURE-3: shows that complications (nasal septal damage: 8% vs 0%), (pneumothorax: 4% vs 0%), (CPAP belly syndrome: 2% vs 0%) were seen only in prophylactic bCPAP group. CLD was in both groups (2% vs 4%). But only septal damage (p-value: < 0.05) showed statistical significance.

The clinical course of the 13 infants who died during the trial period was documented. Among them the six were in the intervention group and seven were in the control group. Eleven infants died of sepsis; three of them had positive blood culture and two of septic infants also developed necrotizing enterocolitis. Two others died of severe respiratory distress syndrome.

DISCUSSION

Several studies suggests that using nasal CPAP as the first intervention in the management of the less severe cases of RDS and restricting MV to the more severe cases may be beneficial in reducing the need for MV and the incidence of chronic lung disease. In the last decade, efforts have been made to improve the survival and long-term outcome of preterm newborns. Prenatal steroid administration has reduced the incidence and severity of RDS. This is one of the few randomized trial studies on the use of Bubble CPAP for the prevention on respiratory distress in preterm infants (gestational age between 28 to 32 weeks). Our study suggested that respiratory outcome in the intervention group, time to improve respiratory distress: (3.14±2.74 vs 3.58±2.12 days, p-value: >0.05); incidence of RDS: 40% (20/50) in the intervention group and 46% (23/50) in the control group (p-value: >0.05); need for surfactant: 20% (10/50) in the intervention group and 28% (14/50) in the control group (p-value: >0.05); 14% (7/50) infants required mechanical ventilator (MV) support in the intervention group in comparison to 18% (9/50) in the control group (p-value: >0.05).

The need for surfactant was 22.6% (26/115) in the prophylaxis group and 21.7% (25/115) in the rescue group (p value: >0.05); the need for MV was 12.2% (14/115) in the prophylaxis group and 12.2% (14/115) in the rescue group (p- value: > 0.05).[14]

Very low birth weight infants with a birth weight of 800-1500 g, the CPAP/InSurE strategy reduced the need for mechanical ventilation compared with treatment with an oxygen hood and early selective surfactant administration followed by mechanical ventilation.[15]

In the recently published COIN trial, early CPAP was used from 5 minutes of life in neonates between 25 and 28 weeks. In the CPAP group, the incidence of death/BPD is significantly less and surfactant use was halved in comparison to the ventilated group of neonates. The CPAP group received significantly fewer days of intubation and ventilation though the incidence of pneumothorax was more in the CPAP group as compared to the ventilated group (9% vs. 3% respectively). Our data suggested that clinical outcome, length of hospital stay in the intervention group: 28.34 ± 12.18 days, in comparison to the control group: 30.74 ± 12.24 days (p-value: >0.05); number of sepsis: 22% (11/50) and 18% (9/50) in the intervention and the control group respectively (p-value: >0.05); number of ROP: 16% (8/50) in the intervention group and 22% (11/50) in the control group (p-value: >0.05).

Length of hospital stay in the intervention group: 30 ± 1 days, in comparison to the control group: 29 ± 1 days; number of sepsis: 19% (16.9/50) and 17% (14.8/115) in the intervention and the control group respectively; number of ROP: 1% (0.9/115) in the intervention group and 0% (0/115) in the control group respectively.[14]

A total of 256 patients were randomized to either the CPAP/InSuE group (n=131) or the Oxygen/MV group (n=125). The need for mechanical ventilation was lower in the CPAP/InSurE group (29.8% vs 50.4%; P = 0.001), as was the use of surfactant (27.5% vs 46.4%; P = 0.002). There were no differences in death, pneumothorax, bronchopulmonary dysplasia, and other complications of prematurity between the two groups.[8]

Our data also suggested that complications of nasal septal damage in the intervention group: 8% (4/50) in comparison to the control group: 0% (0/50) (p-value: >0.05), number of pneumothorax: 4% (2/50) and 0% (0/50) in the intervention and the control group respectively (p-value: >0.05); number of CLD: 2% (1/50) in the intervention group and 4% (2/50) in the control group (p-value: >0.05); CPAP belly syndrome: 2% (1/50) and 0% (0/50) in the intervention and the control group respectively (p value: >0.05). Only nasal septal damage (p value: < 0.05) showed statistical significance.

CONCLUSION

Prophylactic use of Bubble CPAP did not show any significant advantage for the prevention of respiratory distress in preterm infants of 28-32 weeks gestation. Therefore, an unnecessary intervention and its related complications can be avoided in a group of preterm infants who make up a large proportion of admitted babies in NICU. However further multi-centre RCTs with larger sample size could be conducted to strengthen or reject the findings of the current study.

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