Effectiveness of bubble continuous positive airway pressure as a primary mode of respiratory support in preterm neonates with respiratory distress syndrome at district level tertiary care hospital

Sudhakar Ajmera[1], Varunasree Chettipally[2], Vijay Kumar Guduru[3]

From [1]Associate Professor, Department of Pediatrics, [2]Junior Resident, [3]Professor, Department of Pediatrics, Kakatiya Medical College, Warangal, Telangana, India

Correspondence to: Dr. Sudhakar Ajmera, Department of Pediatrics, MGM Hospital, Warangal, Telangana, India. E-mail: 8895sudhakar@gmail.com

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ABSTRACT

Background: Continuous positive airway pressure (CPAP) has become a useful modality in the management of respiratory distress in preterm babies. CPAP when applied to preterm infants with respiratory distress syndrome (RDS) is associated with benefits in terms of reduced respiratory failure and reduced mortality. **Objectives:** The objectives of the study were to evaluate the efficacy of bubble CPAP in preterm neonates with RDS requiring respiratory support and to study the risk factors associated with its failure. **Materials and Methods:** A prospective observational study was done on 243 preterm neonates (gestational age [GA] 28 to <37 weeks) with a diagnosis of RDS admitted from January 2016 to November 2017. All the eligible preterm neonates were started on bubble CPAP with binasal prongs. Surfactant was administered when indicated. **Results:** A total of 243 preterm neonates were enrolled in this study with a mean GA of 32.40 weeks and birth weight of 1831.49 g. One hundred and fifty-one (62.1%) were male and 92 (37.9%) were female. The mean age of starting of CPAP was 13.44 h of life and antenatal steroid coverage was 3.2% only. Of the 243 neonates, 195 neonates were successfully weaned off CPAP. Among the 48 neonates who failed CPAP, 27 neonates were ventilated, of which 20 (74.1%) survived. The predictors of CPAP failure were GA <32 weeks, birth weight <1.5 kg, and delayed initiation of CPAP. **Conclusion:** The efficacy of CPAP in neonates with mild-to-moderate RDS in preterm neonates is very well demonstrated despite the low usage of antenatal steroids, surfactant, and delayed initiation of CPAP. Extreme preterm, very low birth weight neonates with severe RDS on chest X-ray are at risk of failure of CPAP.

Key words: *Continuous positive airway pressure, Neonates, Respiratory distress syndrome*

Continuous positive airway pressure (CPAP) refers to the application of continuous pressure during both inspiration and expiration in a spontaneously breathing baby. CPAP helps in opening of atelectatic alveoli, splints the airways, reduces work of breathing, and improves the pattern and regularity of respiration. Atelectotrauma, biotrauma, and volutrauma, the key determinants of ventilation-induced lung injury are minimal or absent with this mode of ventilation [1].

Underwater bubble CPAP remains in use since first devised in the early 1970s [2]. With this technique, gas flows past the nasal device and the pressure is generated in the circuit by placing the distal limb of the CPAP circuit under a known depth of water. This is a simple and effective technique which can be applied with inexpensive equipment. A unique feature is that the loss of CPAP pressure is detectable by the disappearance of the bubbling.

Apart from pressure, bubble CPAP produces oscillations of up to 4 cm H_2O due to bubbling of water in the bubble chamber. These oscillations act like high-frequency ventilation and may help in gas exchange. It has been suggested that bubble CPAP is more effective than ventilator CPAP due to these oscillations [3]. Bubble CPAP, when used appropriately, is more cost effective, less intensive, requires less training, and has lower risk of complications. It is a less expensive method of respiratory support, most suitable to neonatal units with limited resources in developing countries [4]. The present study was undertaken to assess the effectiveness of bubble CPAP for premature neonates with respiratory distress syndrome (RDS) treated in a tertiary care public sector teaching hospital.

MATERIALS AND METHODS

This prospective observational study was conducted in special newborn care unit in Mahatma Gandhi Memorial Hospital, Kakatiya Medical College, Warangal, from January 2016 to November 2017. A total of 243 preterm neonates with gestational age (GA) between 28 and <37 weeks with respiratory distress (Silverman Anderson Score [SAS] ≥3 in GA <35 weeks and ≥5 in GA >35 weeks) and chest X-ray suggestive of RDS

were included in this study. Neonates with GA <28 weeks and ≥37 weeks, neonates with no spontaneous respiration at birth, and neonates with congenital anomalies such as cleft lip, cleft palate, tracheoesophageal fistula, congenital diaphragmatic hernia, and choanal atresia were excluded from the study. The Institutional Ethical Committee approval was taken before starting the study and parental consent was taken before recruiting the cases.

All the eligible preterm neonates were started on bubble CPAP (Fischer and Paykel) with binasal prongs (Hudson prongs). CPAP was started at 5 cm of water and adjusted to minimize the chest retractions. FiO_2 was adjusted to maintain SpO_2 90–94%. Flow of gas was started at 5 L/min and was adjusted until continuous bubbling was noted in the chamber. Surfactant was administered by intubation-surfactant-extubation method for babies with moderate-to-severe RDS on the chest X-ray showing extensive reticulonodular pattern or complete white-out lung fields.

Preterm neonates with minimal or no chest retractions, having a respiratory rate between 40 and 60/min and normal saturation on FiO_2 <30% and positive end-expiratory pressure (PEEP) <5 cm of water, were weaned off from bubble CPAP. Bubble CPAP was considered to be efficacious if the respiratory distress improved and baby could be successfully weaned off from CPAP. (Baby remains off CPAP for the next 72 h). CPAP failure was defined as the need for mechanical ventilation when they remained hypoxic, i.e., SpO_2 <87% despite FiO_2 >60%, PEEP >7 cm of water or had severe retractions on PEEP >7 cm of water or had recurrent apneas.

Maternal, perinatal, and neonatal data were collected in a predesigned pro forma. GA was calculated based on the mother's last menstrual period or expanded new Ballard score. Based on the radiological findings, severity of RDS was graded as mild – mild granulations of lungs, moderate – generalized granularity of lung with air bronchogram with preserved cardiac borders, and severe – whiteout lungs with loss of cardiac borders.

Appropriate statistical tests were applied using software SPSS version 21. Baseline variables were compared between those who could be successfully weaned from CPAP (CPAP-success group) and those who failed (CPAP-failure group). Mean and standard deviation was calculated for continuous variables and percentages were calculated for categorical variables. Univariate analysis was done to study factors responsible for the failure of CPAP using Student's t-test or Chi-square test or Fisher's exact test as appropriate depending on the variable.

RESULTS

A total of 243 preterm neonates were enrolled in the study with a mean GA of 32.4 weeks and mean birth weight of 1831.49 g. Out of these, 151 (62.13%) neonates were male. Among the study population, 25 mothers had preterm premature rupture of membranes. In this study, 167 (68.72%) were cesarean deliveries and 8 (3.29%) neonates received antenatal steroids. The above results are summarized in Table 1.

Among 243 neonates, 195 (80.2%) were successfully weaned off from CPAP and 48 (19.8%) failed CPAP. The mean birth weight in the CPAP-success group was 2088.71±484.08 g and the CPAP-failure group was 1574.27±596.10 g. The mean GA in CPAP success was significantly higher (33.49±2.24 weeks) than in the CPAP-failure group (31.31±2.78 weeks). The mean age at the beginning of CPAP was lower in success than in the failure group (12.39±11.52 h vs. 14.5±13.38 h). The mean duration of CPAP in the success group was 62.73±30.51 h and in the CPAP failure group was 47.56±53.54 h.

Table 1: Basic demographic features of the study

Variable	Groups	Number (%)
Gestational age (weeks)	28–31	57 (23.45)
	32–34	93 (38.27)
	35–<37	93 (38.27)
Birth weight (g)	≤1000	16 (6.58)
	1001–1500	42 (17.28)
	1501–2000	62 (25.51)
	>2000	123 (50.61)
Gender	Male	151 (62.13)
	Female	92 (37.86)
Maternal condition	PPROM	25 (10.28)
	PIH	19 (7.81)
Type of delivery	Cesarean delivery	167 (68.72)
Antenatal steroid	Yes	8 (3.29)

PPROM: Preterm premature rupture of membranes, PIH: Pregnancy-induced hypertension

Comparison of maternal and neonatal variables between successful and failure groups is shown in Table 2. It was found that lower GA (mean <31 weeks) birth weight <1.5 kg, SAS ≥7, severe RDS on chest X-ray, and presence of sepsis were associated with CPAP failure. Table 3 shows the number of cases in CPAP success and failure groups in relation to the time of initiation of CPAP. Out of 243 babies, only 22 babies received surfactant along with CPAP, as shown in Table 3.

A total of 216 (88.88%) received CPAP alone; out of them, 195 (90.27%) survived and 21 (9.7%) babies expired. Out of 243 babies, 27 (11.11%) babies were kept on ventilation due to CPAP failure. Among 27 ventilated babies, 20 (74.07%) survived and 7 (25.9%) babies died. The most common complication seen in babies put on CPAP was sepsis (66, 27.1%) followed by nasal trauma (45, 18.1%) and shock (3, 1.23%). Periventricular leukomalacia was seen in 2 (0.82%) cases while intraventricular hemorrhage and pneumothorax were seen in 1 (0.41%) neonate each.

DISCUSSION

In our study, 80% of neonates were successfully weaned off from the CPAP and these results were higher than those observed by Koti *et al*. [1] and Urs *et al*. [5]. In the present study, 38.3% of the study population were of 32–34 weeks gestation and another 38.3% of population was of 35–37 weeks gestation. About 50.6% of population was of weight >2000 g, 19.7% were <1500 g, and 4.1% were <1000 g neonates. Urs *et al*. included neonates of GA 28 to <37 weeks (n=50), and 76% of them were of 32–34 weeks

Table 2: Maternal and neonatal variables among neonates with CPAP success and CPAP failure

Variable mean±SD or n (%)	CPAP success (%)	CPAP failure (%)	Mean difference (CI) or *RR (CI)	p value
Total patients	195 (80.2)	48 (19.8)		
Birth weight (g)	2088.71±484.08	1574.27±596.10	0.2 (1.43–0.93)	<0.001
Gestation (weeks)	33.49±2.24	31.31±2.799	514 (353–675)	<0.001
Age at CPAP (h)	12.39±11.52	14.5±13.38	−2.1 (−5.8–1.6)	0.272
CPAP duration (h)	62.73±30.51	47.56±53.54	15.1 (3.6–26.6)	0.009
Male	119 (61.02)	32 (66.66)	1.09 (0.8–1.3)*	0.510
PPROM	16 (8.20)	9 (18.75)	2.29 (1.07–4.8)*	0.059
PIH	14 (7.17)	5 (10.41)	1.4 (0.5–3.8)*	0.547
Antenatal steroid	7 (3.58)	1 (2.08)	0.58 (0.07–4.60)*	1.00
Cesarean delivery	146 (74.87)	21 (43.75)	0.5 (0.42–0.81)*	<0.001
Grade 3 chest X-ray changes	9 (4.61)	13 (27.08)	5.8 (2.6–12.9)*	<0.001
Surfactant	15 (68.2)	7 (31.8)	1.8 (0.81–4.39)*	0.159
Sepsis	43 (22.05)	23 (47.91)	0.46 (0.30–0.68)*	<0.003
SAS<7	166 (85.12)	34 (70.83)	0.8 (0.68–1.00)*	0.033

***Relative risk denotes relative risk for failure of CPAP. CPAP: Continuous positive airway pressure, SD: Standard deviation, SAS: Silverman Anderson score, PPROM: Preterm premature rupture of membranes, PIH: Pregnancy-induced hypertension**

Table 3: Comparison of time (hours) at CPAP started after birth

Variable	Total (243) (%)	Failure (48) (%)	Success (195) (%)
Time after birth at initiation of CPAP (h)			
≤6	120 (49.38)	23 (47.91)	97 (49.74)
7–24	86 (35.39)	13 (27.08)	73 (37.43)
25–72	37 (15)	12 (25)	25 (12.82)
Use of surfactant			
CPAP	221 (90.95)	41 (18.55)	180 (81.44)
CPAP + Surfactant	22 (9.05)	7 (31.81)	15 (68.18)

CPAP: Continuous positive airway pressure

gestation, 66% had birth weight <1500 g, and 8% <1000 g [5]. In a study by Koti *et al*., the study population (n=56) consisted of neonates of GA 28–34 weeks, including 55.3% very low birth weight (VLBW) and 17.9% ELBW neonates. More success rate in the present study compared to these studies may be attributed to larger total sample size with a major portion belonging to neonates with later GA and birth weight >2000 g.

Sandri *et al*. have shown higher need for respiratory assistance in male neonates with RDS. Similar to the study by Urs *et al*., outcome of bubble CPAP did not vary between genders in this study [6]. Statistically significant CPAP success was seen in neonates born to mothers who had received antenatal steroids in a study by Urs *et al*. (p<0.001) and Koti *et al*. (p<0.02). Success was higher in neonates who were given antenatal steroids; however, no such significance was found in studies by Sethi *et al*. and Shamil *et al*. [7,8]. In our study, the percentage of neonates who received antenatal steroids (3.2%) was lower in comparison to other similar studies.

In this study, the mean age at initiation of CPAP was 13.44 h of life, which was higher than that observed in a study by Urs *et al*. (5.5 h). This could be due to delayed presentation of the neonates to this hospital thus delaying the treatment. Cochrane systematic review concluded that the application of CPAP early in the course of the disease as compared to late CPAP was associated with a significant reduction in subsequent use of invasive ventilation [9]. In the present study, CPAP-success rate was more in neonates in whom CPAP was started early (<24 h, p=0.04) similar to the study by Shamil *et al*. (p=0.024).

Verder *et al*. published the first randomized controlled trial of surfactant instillation during CPAP showing that in infants with moderate-to-severe RDS, the need for subsequent mechanical ventilation could be reduced by half after a single dose of surfactant [10]. The effect was more pronounced if the surfactant treatment was given early in the course of the disease [10]. In our study, surfactant was given to 22 babies (9.05%), which was lower in comparison to the results observed by Koti *et al*. (55.3%) [1] and Sethi *et al*. (41.4%) [7].

In the present study, 48 (19.8%) out of 243 neonates were considered as CPAP failure, of which 20 neonates were ventilated and 28 neonates (11.5%) died. Mortality rate was more in preterm neonates with GA 28–31 weeks (8.64%, n=21) and neonates with birth weight <1500 g (8.23%, n=20). The high mortality rate in this study compared to the study by Koti *et al*. (10.7%) may be explained by inadequate usage of antenatal steroids, delay in initiation of CPAP, and lesser use of surfactant. Indian studies on CPAP have shown a failure rate of 25–50%. There were few limitations of this study. There was no monitoring protocol for the patients on CPAP.

CONCLUSION

The efficacy of CPAP in neonates with mild-to-moderate RDS in moderate preterm neonates is very well demonstrated despite the low usage of antenatal steroids, surfactant, and delayed initiation of CPAP. Extreme preterm neonates, VLBW neonates with severe RDS on chest X-ray are at risk of failure of CPAP.

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