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Failure Factors of Bubble CPAP in Neonates with Respiratory Distress

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Abstract

Background: Respiratory distress is the most frequent presenting complaint of newborn encountered within the first 48–72 hours of life. An infant who is breathing on instinct is given non-invasive respiratory support called Bubble Continuous Positive Airway Pressure (Bubble CPAP) to help them to maintain a long volume during expiration. The study aimed to identify failure factors of Bubble CPAP in neonate with respiratory distress. **Material & Methods:** From April to September 2017, a cross-sectional study was carried out at the Department of Neonatal Medicine in Bangladesh Shishu Hospital & Institute. One hundred and eight (N=108) newborns with respiratory distress who were given Bubble CPAP were enrolled for the study. After receiving the parent's or guardian's written informed consent, all the necessary information were recorded in a predesigned proforma that included the patient's specifics. Then completed data forms were reviewed, updated, and prepared for computer data input. The "t" test, "r" test and Statistical Package for the Social Sciences (SPSS) Version 23.0 were used to analyze the data. **Results:** Among study patients (N=108), most of the neonates 49 (45.4%) belonged to age ≤24 hours and the neonates with respiratory distress which needed Bubble CPAP support 18 (16.7%) had RDS, 18 (16.7%) had PNA, 15(13.9%) had pneumonia, 14(13.0%) had PPHN, and 10(9.3%) had sepsis. More than three-fourths of the patients (85) were found successfully weaned and one-fifth of the patients (23) failed. **Conclusion:** The most frequent causes of respiratory distress were RDS, PNA, PPHN, Sepsis, congenital pneumonia, and pneumonia. Grunting respiration, higher RR, lower SPO2, higher FiO2 and cyanosis were substantially associated with Bubble CPAP failure among the respiratory distress symptoms. PPHN and sepsis have a causal relationship with Bubble CPAP failure. More duration of Bubble CPAP and more hospital stay also have relation with Bubble CPAP failure. The majority of patients were weaned, however, patients who failed Bubble CPAP died more frequently.

Keywords:- Respiratory Distress, Neonate, Bubble CPAP, failure factor, Sepsis, PPHN.

INTRODUCTION

For infants, Bubble CPAP is a tried-and-true method of respiratory assistance.[1] Bubble CPAP is a low-cost nasal CPAP delivering system with an underwater seal that causes chest vibration due to gas flow underwater.[2] These vibrations stimulate waveforms produced by high-frequency ventilation.[3] Gregory et al. first pioneered the use of Bubble CPAP in Neonatology with their landmark paper in the 70s in Columbia.[4]

The Bubble CPAP generator is a cylindrical, transparent bottle filled to a predetermined level with distilled water. The expiratory limb

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of the circuit is immersed in this bottle, and the depth of the immersion in centimeters below the water surface corresponds to the desired Bubble CPAP in cm of H2O, usually between 5 cm to 8 cm of H2O.[5,6,7] This provides positive pressure in the whole respiratory cycle, increases the functional residual capacity of the lungs, and lowers the work of breathing.[8] Ultimately, Bubble CPAP reduces the need for mechanical ventilation, morbidity, and mortality.[9,10] Many studies have shown that locally manufactured Bubble CPAP systems showed promising results.[11] Besides, it is more acceptable for its simplicity, low cost, and yet a powerful and effective technique of respiratory support, particularly suitable for neonatal units with limited resources.[12]

Arora et al studied to ascertain the immediate outcome of preterm infants with respiratory distress syndrome (RDS) on Bubble CPAP and identified risk factors associated with its failure.[13,14] 170 neonates were enrolled in this study, and 52 (30.5%) babies failed Bubble CPAP. The predictors of failure were partial or no response to Antenatal Steroids (ANS), white-out on the chest X-ray, Silverman Anderson scoring >6, or FiO_2 > 0.4 after 15-20 minutes of Bubble CPAP and extreme prematurity. Rates of mortality and duration of oxygen requirement were significantly higher in babies who failed Bubble CPAP. Infants with no or partial exposure to antenatal steroids, white-out chest X-ray, and those with higher FiO_2 requirements after initial stabilization were at increased risk of Bubble CPAP failure (mechanical ventilation needed).

Koti et al also investigated the immediate results of premature newborns with RDS using Bubble CPAP and found risk factors for its failure.[9] This study explained that Bubble CPAP failures-infants required mechanical ventilation in the first week. 56 neonates were enrolled in the study and 14 (25%) babies failed Bubble CPAP. The predictors of failure were no or only partial exposure to antenatal steroids, white-out on the chest X-ray, patent ductus arteriosus, sepsis/ pneumonia, and Downe's score >7 or FiO_2 ≥50% after 15- 20 minutes of Bubble CPAP. Rates of mortality and duration of oxygen requirement were significantly higher in babies who failed Bubble CPAP. Only two infants developed pneumothorax. However, infants with no or partial exposure to antenatal steroids, white-out chest X-ray, patent ductus arteriosus, sepsis/pneumonia, and those with higher FiO_2 requirement after initial stabilization were at high risk of Bubble CPAP failure (mechanical ventilation needed).

Soomro and Tikmani assessed to observe the survival of preterm infants with RDS treated with Bubble CPAP. Multivariable analysis showed there, such as weight of an infant less than 1.5 kg (OR 8.63, 95% CI: 1.71-43.57), respiratory rate of >70 breaths per minute (OR 9.59, 95% CI: 2.59-35.52), nasal flaring (OR 3.35, 95% CI: 1.08-10.31) and typical findings of RDS on chest X-rays (OR 12.04, 95% CI: 1.89-76.52) were independent risk factors for failure of Bubble CPAP. However, gestational age (OR 0.70, 95% CI: 0.54-0.89) is protective against failure factors.[13]

A prospective observational study was done by Mathai et al,[15] on 50 preterm babies requiring respiratory support for mild to moderate respiratory distress. RDS was the most typical indication found in 30 babies out of 50. The mean maximum pressure was 6.04 cm of H_2O, and the mean maximum FiO_2 was 72.16%. Mean

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maximum PaO_2, $PaCO_2$, and mean minimum $PaCO_2$ were 92.93 mm Hg (±16.97), 52.36 mm Hg (±7.78), and 36.46 mm Hg (±4.95), respectively. Late initiation had a statistically higher incidence of failure. The failure rate was 30%, and the survival rate was 94%.

Another scientist Sharba et al,[16] studied to evaluate the effectiveness of using Bubble CPAP in managing RDS and identified the risk factors associated with its failure. Preterm neonates with extremely low birth weight, lower gestational age, multiple pregnancies (twin or triple), white-out on the chest X-ray, delay in the application of Bubble CPAP, and prolonged treatment duration had an increased risk for its failure. Sepsis, apnoea, and shock are the primary immediate complications of RDS patients, adversely affecting the Bubble CPAP success.

Another prospective observational study was done by Sethi et al,[3] that expressed 51 babies, both term and preterm, admitted to the NICU of SMIMER Hospital, Surat, India, requiring respiratory support for mild to moderate respiratory distress. The most common disease for starting Bubble CPAP was RDS (80%), followed by pneumonia (17%), TTNB (0%), and MAS (2%). The commonest complications of Bubble CPAP were shock, apnoea, and nasal damage. The overall failure of Bubble CPAP occurred in 21 cases out of 51 patients (40%). All babies who failed Bubble CPAP were put on mechanical ventilation. Failures in the RDS group were 18 out of 41(43%). The failure rate in the pneumonia group was 3 out of 9 (33.3%). Higher cases of sepsis and pulmonary hemorrhage were seen in the failure group. The overall survival rate of the study population was 60%. By identifying failure factors of Bubble CPAP, this report drew attention to taking measures to minimize Bubble CPAP failure in neonates with respiratory distress.

MATERIAL AND METHODS

This cross-sectional study was conducted at the Department of Neonatal Medicine at Bangladesh Shishu (Children) Hospital and Institute in Dhaka, Bangladesh, from April 2017 to September 2017.

Neonates with respiratory distress admitted at the Department of Neonatology in Bangladesh Shishu Hospital were enrolled. Both term and preterm neonates with respiratory distress who had two or more of the following findings were included in the study: respiratory rate >70/min, grunting respiration, cyanosis, moderate to severe intercostal retractions, supraclavicular & suprasternal retractions, and oxygen saturation in the pulse oximeter less than 85%. Neonates with type II respiratory failure, congenital heart disease, anatomical abnormalities of the lungs and GI tract that caused respiratory distress at delivery, and neonates who required intubation at birth were excluded from the study.

Sample size has been calculated with the following formula:

$$n = \frac{Z^2pqN}{e^2 (N-1) + Z2pq}$$

Here,
Z = 1.96 [at 5% level of significance or 95% confidence interval (CI)]
p = 50% (0.5) [as prevalence is not known]
q = (1 - p) = 50% (0.5)
e = 10% of p (0.5) = 0.05
N = 150 (Neonate with severe respiratory distress admitted in Neonatology dept. of DSH

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in 6 months). According to above formula, n=108.

Operational Definition: Maximum Bubble CPAP Support criteria was FiO2 – 70-90 % and PEEP – 7-8 cm of H2O.

Following written parental or guardian agreement, pertinent data was entered into a predesigned proforma that covers the patient's specifics, such as age at admission, sex, birth weight, gestational age, and mode of delivery. The results of the examination were then recorded, including measurements of the subject's weight, length, OFC, heart rate, respiration rate, temperature, CRT, consciousness status, pallor, jaundice, cyanosis, dehydration, chest retraction, tone, and primitive reflexes. Pulse oximetry was used to determine oxygen saturation. Requirement of inotrope was noted. Investigation findings such as RBS, CXR and ABG were also recorded.

After fulfillment of enrollment criteria patients were put into Bubble CPAP and monitoring was done clinically, with pulse oximetry and ABG for requirement of change in settings to observe failure. Weaning was done in absence of respiratory distress (Minimal or no retraction and respiratory rate between 30 and 60 per min) and SpO2>90% with PEEP < 5 cm of H2O and FiO2< 50%.

Failure of Bubble CPAP was considered when neonate remained hypoxia with SpO2<87% with FiO2 > 70% and PEEP >7cm of H2O, had severe retractions on PEEP >7cm of H2O, PO2<60 mmHg, PCO2>60 mm Hg and pH <7.25 on maximum acceptable settings, had prolonged (>20 seconds) or recurrent apneas (>2 episodes within 24 hours associated with bradycardia) requiring bag and mask ventilation, had severe metabolic acidosis or shock requiring inotropic support (dopamine and or dobutamine) >20µg/kg/min. The results of those who failed Bubble CPAP were identified and recorded. Failure-related factors were also investigated.

The Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA) was used to conduct the statistical analyses. The mean values for continuous variables were determined. Frequencies and percentages were used to denote the quantitative observations. The categorical variables displayed with cross-tabulation, were analyzed using the Chi-Square and Fisher's exact tests. The continuous variables were analyzed using paired and unpaired t-tests. Statistics were considered significant for P values under 0.05.

RESULTS & DISCUSSION

In this study we found that among 108 neonates 62(57.4%) patients were male and 46(42.6%) patients were female. The ratio was 1.3:1 male to female. It was observed that the majority 49(45.3%) of patients belonged to age ≤24 hours. The following table shows the age, sex, birth weight, gestational age and mode of delivery of the study patients.

We noticed that 102(94.4%) patients had chest retraction followed by 85(78.7%) had tachypnoea, 57(52.8%) had cyanosis, 53(49.1%) had H/O apnoea and 41(38.0%) had pallor [Figure 1].

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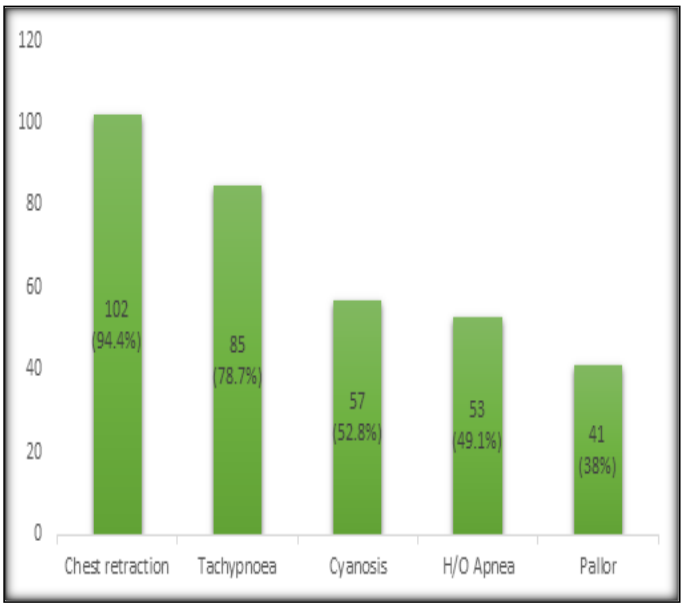

Figure 1: Bar chart presentation of the study patients according to clinical features (n=108)

With a range of age of 2 to 204 hours, the mean age was found to be 43.3±43.1 hours. Two-third 72(66.7%) patients were having birth weight ≥ 2500gm, 22(20.4%) patients having 1500-2499gm and 14(12.9%) patients having <1499gm. Regarding gestational age of the study patients, majority 64(59.3%) patients belonged to the age between 37-41 weeks, along with 27 patients (25%) were between 33-36 weeks and 17 patients (15.7%) who were between 28-32 weeks. Besides, 63 patients (58.3%) were delivered by LUCS while 45 (41.7%) were by NVD.

Besides, we discovered that among the patients, 14(13.0%) had PPHN, 15(13.9%) had Pneumonia, 18(16.7%) had RDS, and 18(16.7%) had PNA [Table 2]. According to this, RDS, PNA, PPHN, Pneumonia, Congenital Pneumonia, and Sepsis were the most common illnesses for commencing Bubble CPAP in neonates with respiratory distress. Out of 23 failed cases, 6(26.1%) had PPHN and another 6(26.1%) had Sepsis. PPHN and Sepsis were statistically significant ($p<0.05$) when compared to outcome of Bubble CPAP. So, PPHN and Sepsis has association with Bubble CPAP failure.

Table 1: Distribution of the study patients according to Sex, Age, Birth weight, gestational age and mode of delivery (n=108).

<table>
<tr><th>Sex</th><th colspan="3">Age</th><th colspan="3">Birth Weight</th><th colspan="3">Gestational Age</th><th>Mode of delivery</th></tr>
<tr><td rowspan="2">Male
62
(57.4%)</td><td>Hours</td><td>No of Patients</td><td>%</td><td>gm</td><td>No of Patients</td><td>%</td><td>Weeks</td><td>No of patients</td><td>%</td><td rowspan="2">NVD
45
(41.7%)</td></tr>
<tr><td>≤24</td><td>49</td><td>45.3</td><td rowspan="5"><1499
1500
-2499

≥2500</td><td rowspan="5">14</td><td rowspan="5">12.9</td><td>28-32</td><td>17</td><td>15.7</td></tr>
<tr><td>25-48</td><td>23</td><td>21.3</td><td>33-36</td><td>27</td><td>25.0</td><td rowspan="3">LUCS
63
(58.3%)</td></tr>
<tr><td rowspan="3">Female
46
(42.6%)</td><td>49-72</td><td>15</td><td>13.1</td><td>37-41</td><td>64</td><td>59.3</td></tr>
<tr><td>>72</td><td>21</td><td>19.4</td><td colspan="3" rowspan="2">Total
108
100.0</td></tr>
<tr><td colspan="3">Mean ±SD

43.3±43.1

Range (min-max) 2-204</td></tr>
</table>

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Table 2: Association between outcome of Bubble CPAP with diagnosis.

Diagnosis	Weaned (n=85)		Failed (n=23)		P value
	n	%	n	%	
RDS	15	17.6	03	13.0	0.43ns
PNA	17	20.0	01	4.3	0.06ns
PPHN	8	9.4	06	26.1	0.04s
Congenital Pneumonia	11	12.9	02	8.7	0.44ns
Pneumonia	12	14.1	03	13.0	0.60ns
Sepsis	4	4.7	06	26.1	0.006s

s=significant, ns= not significant
P value reached from chi square test

Table 3: Association of respiratory characteristics at the time of enrollment for Bubble CPAP.

Risk factors	Weaned (n=85)		Failed (n=23)		P value
	n	%	n	%	
Cyanosis	38	44.7	19	82.6	0.001^{s}
Grunting respiration	45	52.9	19	82.6	0.010^{s}
Chest retraction	82	96.47	21	91.30	0.28^{ns}
	Mean±SD		Mean±SD		
SPO2 (%)	80.22±7.83		57.69±14.59		<0.001
RR (breaths/min)	67.88±5.86		71.04±6.76		0.02

s= significant, ns= not significant,
P value reached from chi square test and unpaired t-test

Table 4: Comparison of mean PEEP and FiO2 at starting between weaned and failed group

Patient's condition	PEEP at starting (cmH2O)	P value
Wean	6.08(±0.74)	<0.001^{s}
Failure	6.73 (±6.73)	<0.001^{s}
Patient's condition	FiO2 at starting (%)	P value
Wean	64.58(±10.06)	0.02^{s}
Failure	69.56 (±8.77)	<0.001^{s}

Table 5: Comparison of blood gas changes at starting between weaned and failed group

Blood Gas Variables	Wean Mean (±SD)	Failure Mean (±SD)	P value
pH at starting	7.34±.08	7.29±0.05	0.001^{s}
PO2 at starting (mmHg)	104.29±46.89	52.37±7.50	<0.001^{s}
PCO2 at starting (mmHg)	28.86 ±8.07	27.21 ±6.57	0.36^{ns}
HCO3 at starting (mmol/L)	16.91 ±5.72	14.60 ±3.67	0.07^{ns}

s=significant; ns= not significant
P value reached from unpaired t-test

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Table 6: Distribution of the study patients according to admission time to Bubble CPAP, duration of Bubble CPAP and hospital stay (n=108)

Time from admission to Bubble CPAP (hours)	**Number of patients**	**Percentage**
≤12	42	38.9
>12-24	40	37.0
>24-48	25	23.2
>48	1	0.9
Duration of Bubble CPAP (hours)	Number of patients	Percentage
≤ 24	15	13.9
25-48	53	49.1
>48	40	37.0
Hospital stay (days)	Number of patients	Percentage
1-7	73	67.6
>7	35	32.4

Table 7: Distibution of duration of Bubble CPAP, hospital stay, time from admission to Bubble CPAP and outcomes

Variables	**Wean Mean (±SD)**	**Failure Mean (±SD)**	
Duration of Bubble CPAP (hour)	48.17±.24.17	54.17±24.63	0.001^{s}
Hospital stays (Day)	6.60±2.29	5.86±2.68	$<0.001^{s}$
Time from admission to Bubble CPAP	17.03±9.65	23.43±17.29	0.36^{ns}

s= significant; ns=not significant
P value reached from unpaired and chi square test

This study reported that 85 (78.7%) patients were effectively weaned, compared to 23 (21.3%) who failed. In the weaning group, 38 (44.7%) patients and 19 (82.6%) in the failed group showed cyanosis. Among the target patients, cyanosis was present in 38 (44.7%) patients in weaned group and in 19 (82.6%) patients in failure group. Grunting respiration was observed in 45 (52.9%) patients in weaned group and in 19(82.6%) patients in failure group [Table 3]. That means the patients with cyanosis and grunting respiration during enrollment failed more.

The mean Initial SPO_2 was 80.22±7.83 in failed group and 57.69±14.59 in weaned group respectively which is statistically significant [Table 3]. So, we can say lower SPO_2 increases the chance of failure. The mean initial RR was 67.88±5.86 breaths/min and 71.04±6.76 breaths/min in weaned and failed groups respectively. The differences between the two groups were statistically significant ($p<0.05$). Therefore, the patients with higher RR failed more frequently.

PEEP was found to start at 6.08±0.74 cm of H_2O in the weaning group and 6.73 ±6.73 cm of H_2O in the failure group [Table 4]. A statistically significant difference existed ($p<0.05$). This indicates that initial PEEP in the failed group was higher than in the weaning group. Patients who initially required more PEEP have a higher risk of failing.

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Similarly, starting FiO_2 was found 64.58±10.06% in weaned group and 69.56±8.77% in failed group [Table 4]. Both were statistically significant. Therefore, the chances of failure are higher for patients who need greater FiO_2 from the beginning. That means higher starting PEEP and FiO_2 both are related to Bubble CPAP failure.

Regarding blood gas, pH at starting in wean group and failure group were 7.34±.08 and 7.29±0.05 respectively [Table 5]. On the other hand, PO_2 at starting in wean group was 104.29±46.89 whereas, in failure group was 52.37±7.50. Both values were statistically significant (table 5). In failure group starting pH and PO_2 were less than in wean group which means the patients who had lower pH and PO_2 at starting failed more.

Following [Table 6], shows time from admission to Bubble CPAP, duration of it and hospital stay days of the study patients. It was observed that majority (38.9%) patients were put into Bubble CPAP within ≤12 hours, 40(37.0%) were within >12-24 hours, 25(23.1%) were within >24-48 hours and 1(0.9%) were within >48 hours of admission.

53(49.1%) patients required Bubble CPAP for 25-48 hours, whereas 15(13.9%) patients needed ≤24 hours and 40(37.0%) patients needed >48 hours. So, for most of the patient's duration of Bubble CPAP was 25-48 hours. Regarding hospital stay of the study patients, it was observed that more than two third 73(67.6%) patients had 1-7 days of hospital stay and 35(32.4%) had >7 days of hospital stay.

We observed the association of duration of Bubble CPAP and hospital stay were statistically significant ($p<0.05$) between two groups. That means more duration of Bubble CPAP and more hospital stay have relation with the failure.

CONCLUSIONS

The most frequent causes of respiratory distress were RDS, PNA, PPHN, Sepsis, Congenital pneumonia, and Pneumonia. Grunting respiration, higher RR, lower SPO2, and cyanosis were substantially associated with Bubble CPAP failure. PPHN and Sepsis have a causal relationship with Bubble CPAP failure. Its failure was also significantly correlated with increased metabolic acidosis, hypoxia, and decreased PEEP and FiO2 initially. More duration of Bubble CPAP and more hospital stay also have relation with Bubble CPAP failure. The majority of patients were weaned, however, patients who failed Bubble CPAP died more frequently.

Limitations and Recommendations

It was a small-scale study (among 108 neonates) carried out over a short period at a single location. There is no obstetric unit at Bangladesh Shishu Hospital and Institute because it is a pediatric hospital. As a result, candidates for Bubble CPAP occasionally arrive later at the institute. A large-scale, multi-center investigation in an extended time needs to achieve the goal of the study.

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