ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

USE OF EARLY CPAP IN PRETERM NEONATES WITH HYALINE MEMBRANE DISEASE

[1]Dr Aishwarya Singh, [2]Dr Saurabh Piparsania

[1]PG Resident, [2] Professor; Department of Pediatrics, Index Medical College Hospital & Research Center, Indore

Abstract

Introduction: Hyaline Membrane Disease (HMD) is a major cause of respiratory distress in preterm neonates due to a deficiency in pulmonary surfactant. Continuous Positive Airway Pressure (CPAP) serves as an effective non-invasive respiratory support that can reduce the necessity for invasive ventilation. This study evaluated the efficacy and outcomes of nasal CPAP in preterm neonates with HMD.

Materials & Methods: After receiving IEC approval, a 12-month retrospective and prospective observational study was conducted. The study involved 50 intramural neonates, aged 28-36 weeks gestation, admitted to the NICU at IMCHRC with clinical and radiological signs of HMD. These neonates were treated with nasal CPAP and categorized into two groups: CPAP success (weaned off CPAP) and CPAP failure (required mechanical ventilation). Statistical analyses compared outcomes between these groups.

Results: Among 227 preterm deliveries, 62 inborn neonates were diagnosed with HMD, and 50 received CPAP within 0-6 hours of birth. CPAP was successful in 82% of cases, while the remaining 18% required advanced ventilation. The mean CPAP duration was 37.5 ± 15.40 hours for the success group and 9.2 ± 1.56 hours for the failure group. CPAP effectiveness was 100% for mild, 93.10% for moderate, and 46.67% for severe HMD. Furthermore, 90% of those needing ventilation were under 32 weeks gestation.

Conclusion: In developing countries, where prematurity and limited antenatal steroid use increase HMD risk, early nasal CPAP effectively treats mild to moderate HMD but is less effective for severe cases. It offers a safe, cost-effective alternative to invasive ventilation, reducing mechanical ventilation requirements, hospital stays, complications, and mortality.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Keywords: Hyaline membrane disease, respiratory distress, CPAP

Introduction

Respiratory distress syndrome (RDS) is the leading cause of respiratory distress in preterm infants, largely due to a deficiency in pulmonary surfactant [1,2]. This deficiency causes elevated surface tension in immature lungs, leading to alveolar collapse, atelectasis, uneven lung inflation, and over-distension of alveoli at the end of expiration. In cases of hyaline membrane disease (HMD), clinical symptoms typically appear gradually within the first few hours after birth. Breathing movements in surfactant-deficient lungs create shear forces that damage the epithelium of the terminal bronchioles, resulting in epithelial lesions. This allows fibrinogen and other serum proteins to leak into the alveoli, inhibiting surfactant function and causing progressive alveolar collapse [3], which characterizes RDS [4]. The incidence of RDS is higher with lower gestational age, reaching nearly 80% in infants born before 28 weeks.

Continuous distending pressure (CDP), such as CPAP, is employed to prevent and treat RDS, manage apnea, and assist in weaning from invasive positive pressure ventilation (IPPV). CPAP facilitates the recruitment of collapsed alveoli, reduces intrapulmonary shunt [5], increases functional residual capacity (FRC), and enhances gaseous exchange. It decreases inspiratory resistance by dilating airways, allowing for a larger tidal volume at a given pressure, thus reducing the work of breathing [6]. CPAP also regularizes and slows the respiratory rate, raises mean airway pressure, improves ventilation-perfusion mismatch, and conserves surfactant on the alveolar surface [7,8].

CPAP can be administered via a face mask, nasopharyngeal tube, or nasal prongs, using conventional ventilators, bubble circuits, or CPAP drivers. Bubble CPAP, a newer system, uses an underwater seal to generate vibrations transmitted to the infant's airway. These vibrations mimic the waveforms produced by high-frequency ventilation [9].

Methodology

After obtaining approval from the Institutional Ethics Committee (IEC), a retrospective and prospective observational study was conducted over a 12-month period i.e., from J from June 2022 to June 2023. The study included 50 intramural neonates, aged between 28-36 weeks

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

gestation, admitted to the NICU at IMCHRC with clinical and radiological signs of Hyaline Membrane Disease (HMD). An informed written consent was taken from all selected patients after explaining the protocols and objectives of the study in their vernacular language.

Inclusion Criteria:

- Preterm newborns between gestational age of 28 -34wks admitted in NICU,
- Neonates with Respiratory distress (Modified Downes Score 5-8) within 6 hrs after birth, with evidence of HMD and
- Neonates with Skiagram of chest showing either poor expansion with air bronchogram or reticulogranular pattern or ground glass opacity.

Exclusion Criteria

- All term neonates (>37 weeks age),
- Neonates with congenital malformations or anomalies of airway like choanal atresia, cleft palate, tracheoesophageal fistula and congenital diaphragmatic hernia,
- Babies born to mothers receiving general anaesthesia, phenobarbitone, Pethidine and other drugs likely to depress the baby,
- Preterm born outside our hospital,
- Babies with meconium aspiration syndrome & birth asphyxia

Methodology

The study followed Institutional Ethical Committee guidelines and assessed respiratory distress using the Modified Downes score, which measures respiratory rate, oxygen requirement, retraction, grunting, breath sounds, and air entry. Neonates were treated with nasal CPAP and categorized into two groups: the CPAP success group (those weaned off CPAP) and the CPAP failure group (those who required mechanical ventilation). Neonates who did not respond to CPAP were subsequently transitioned to mechanical ventilation.

Statistical Analysis

Data were coded and entered into Microsoft Excel 2010 and analyzed using both Excel 2010 and SPSS 20.0 for Windows. Quantitative data were described as means ± standard

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

deviation, with differences assessed using Student's t-test or ANOVA. Neonates successfully weaned off CPAP were categorized as the CPAP success group, while those requiring mechanical ventilation were the CPAP failure group. Statistical analysis included comparing proportions with the chi-square (χ^2) test and mean differences with the Student's t-test. Results were presented as absolute numbers, percentages, and averages (mean ± SD) for parameters like duration of treatment, age at admission, age at treatment, and ABG values. A p-value of <0.05 was deemed statistically significant.

Results

Total number of deliveries and preterm births (<37 weeks) and incidence of Hyaline Membrane Disease (HMD) in Index Medical College Hospital & Research Centre, Indore during the study period i.e., from June 2022 to June 2023 were determined

- Total number of deliveries: 1822
- Total number of preterm neonates (<37 weeks): 227
- Incidence of preterm neonates: 12.4%
- Total number of diagnosed HMD cases: 62
- Incidence of HMD in neonates with gestational age between 28-34 weeks: 3.4%
- CPAP was administered to 50 babies from period of 0-6 hrs of birth.

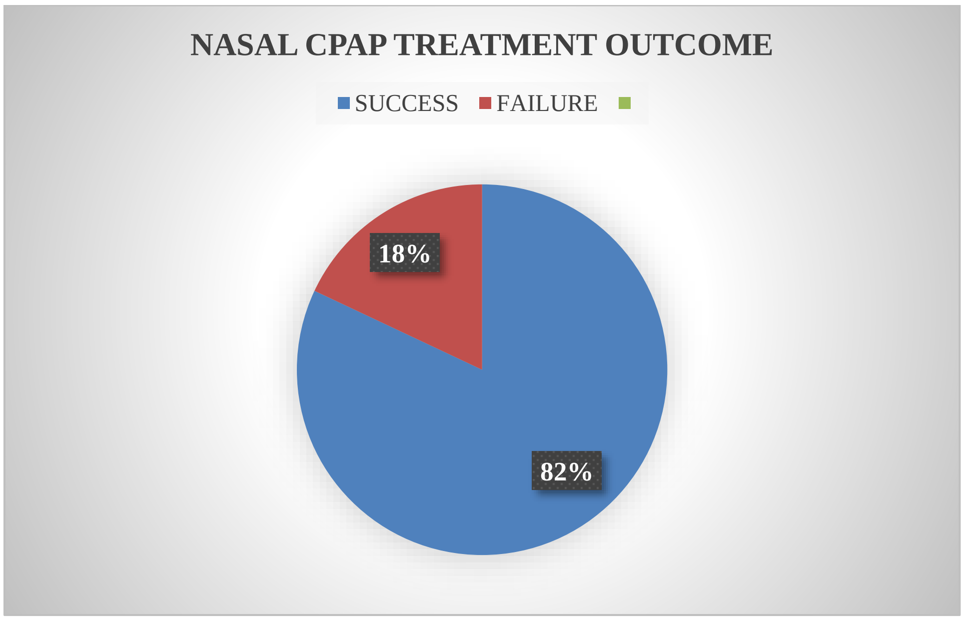
Sex	**Total no. of babies n (%)**
MALE	34 (68%)
FEMALE	16 (32%)
Gestational age	
28-30wks	13 (26%)
31-34wks	37 (74%)
Birth weight (gms)	
<1000gms	24(48%)

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

>1000gms	26(52%)

Table 1. Distribution based on gender, gestational age, birth weight, antenatal steroids

Graph 1 shows the outcome in study group after early nasal CPAP. Among 50 babies, 41 improved with success rate of 82%, 9 (18%) babies failed requiring higher mode of ventilation.



Graph 1: Nasal CPAP treatment outcome among babies

Table 2 illustrates the gender distribution among the study group, revealing a success rate of 78.1% (25) for males and 88.88% (16) for females in the CPAP treatment.

Gender	Success	Failure	Total
Male	25 (78.1%)	7 (21.9%)	**32**
Female	16 (88.8%)	2 (11.11%)	**18**
	41	9	**50**
χ^2 = 1.38	**df=1**	**p>0.05 Not significant**	

Table 2: Gender distribution among study group

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Table 3 shows that higher the gestational age more is the success rate with statistically significant difference between success & failure groups.

Table 4 showed that the ideal duration to wean off from CPAP was determined from the above results documented. The mean duration in success group was 37.5±15.4 hours with range being 10-72 hours. Similarly mean duration of treatment in failure group was 9.2±1.56 hours range being 8-12hours.

Gestational age (weeks)	Total	Success	Failure
28-30	13	7 (53.8%)	**6 (46.2%)**
31-32	29	27 (93.1%)	**2 (6.9%)**
33-34	8	7 (87.50%)	**1 (12.50%)**
	50	41 (82%)	**9 (18%)**
χ^2 =14.45	**df=2**		**p>0.001 Not significant**

Table 3: Effect of CPAP on babies based on gestational age

Group	Number	Hours (range)	Mean ±*SD*
Success	40	10-72	37.5± 15.40
Failure	10	8-12	9.2± 1.56

Table 4: Effectiveness of CPAP based on time (mean duration of treatment in hours)

Out of the 17 babies with an initial SA score of 4, 6 improved to score 2, 7 improved to score 3, and 4 deteriorated to a score of 6, necessitating ventilation. Among the 33 babies with a score of ≥5 before receiving nasal CPAP, 2 improved to a score of 2, 17 improved to a score of 3, and 8 improved to a score of 4 after 6 hours of nasal CPAP treatment. This demonstrates a statistically significant improvement in SA scores with early nasal CPAP (Table 5).

Total no.of babies	SA score before CPAP	SA score after 6hours of CPAP				
		2	**3**	**4**	**6**	**7**
17	**4**	6(35.2%)	7(41.1%)	0	4(23.7%)	**0**

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

33	**≥5**	2(6.1%)	17(51.5%)	8(24.2%)	5(14.7%)	1(3.5%)
50		8(16%)	24(48%)	8(16%)	9(18%)	1(2%)
χ^2 =23.50		**df=8**		**p<0.005 (significant**		

Table 5: Effect of CPAP on SA (Silverman Anderson) score

Table 6 demonstrates the positive impact of CPAP on neonates by showing significant improvements in oxygenation and bicarbonate levels. In the CPAP success group, the analysis of ABG parameters revealed an increase in pH levels from 7.16 ± 0.069 to 7.36 ± 0.0, although not statistically significant ($p = 0.168$). PO2 levels significantly rose from 56.64 ± 11.28 mmHg to 80.48 ± 7.5 mmHg, reflecting improved oxygenation ($p = 0.659$). PCO2 levels dropped from 41.31 ± 11.14 mmHg to 30.62 ± 6.6 mmHg, indicating better ventilation ($p = 0.270$). Bicarbonate levels also increased from 18.37 ± 0.97 mmol/L to 20.50 ± 1 mmol/L, showing enhanced acid-base balance, though this was not statistically significant. In contrast, the CPAP failure group showed no significant change in pH levels (7.31 ± 0.109 to 7.31 ± 0.118, $p = 0.073$). However, PO2 levels dropped significantly from 55.43±10.46 mmHg to 42.16 ± 18.83 mmHg ($p = 0.001$), indicating inadequate oxygenation. PCO2 levels slightly increased from 36.99 ± 10.42 mmHg to 38.40 ± 9.73 mmHg ($p = 0.036$), signifying insufficient ventilation, and bicarbonate levels decreased from 18.56 ± 0.81 mmol/L to 17.15 ± 0.83 mmol/L ($p < 0.001$), indicating worsening acidosis. These results suggest that nasal CPAP is effective in treating mild to moderate Hyaline Membrane Disease (HMD) in preterm neonates. However, for severe cases, CPAP alone is inadequate, highlighting the need for mechanical ventilation to manage worsening respiratory distress and maintain acid-base balance.

Table 7 shows the result therefore suggests the usefulness of CPAP in mild and moderate HMD babies. In severe grade HMD the success rate was only 46.67%.

The study found a significant difference in CPAP success rates between neonates whose mothers received antenatal steroids and those who did not. Specifically, the success rate was 93.1% in babies born to mothers who had received antenatal steroids, compared to only 66.7% in those whose mothers had not received them. This difference is statistically significant ($p < 0.05$), suggesting that antenatal steroids play a crucial role in improving outcomes for Hyaline Membrane Disease (HMD) when treated with CPAP. Thus, administering antenatal steroids to

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

mothers appears to contribute to a more favorable prognosis for preterm neonates with HMD. (Table 8)

ABG parameters	**Before early nasal CPAP mean± *SD***		**After early nasal CPAP Mean ± *SD***	
	Success	**Failure**	**Success**	**Failure**
pH	7.16±0.069	7.36±0.109	7.37±0.0	7.31±0.118
't' value	1.433		2.00	
'p' value	0.168		0.073	
PO2	56.64±11.28	55.43±10.46	80.48±7.5	42.16± 18.83
't' value	0.451		6.309	
'p' value	0.659		0.001	
PCO2	41.31±11.14	36.99±10.42	30.62±6.6	38.40±9.73
't' value	1.147		2.389	
'p' value	0.270		0.036	
HCO $^{-}$3	18.37±0.97	18.56±0.81	20.50±1	17.15±0.83
't'value	0.64		10.82	
'p'value	>0.05		<0.001	

Table 6: Effect of CPAP on ABG analysis

HMD grading	**Success**	**Failure**	**Total**
Mild	6 (100%)	0	6
Moderate	27(93.10%)	2(6.9%)	29

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Severe	7(46.67%)	8 (53.33%)	15
	40	10	50

Table 7: Effect of CPAP on babies categorized based on HMD

Steroids received	Success	Failure	Total
YES	27 (93.1%)	2(6.9%)	**29**
NO	14(66.7%)	7(33.3%)	**21**
	41	9	**50**
χ^2 =22.50	**df=1**	**p<0.05, Significant**	

Table 8: Effect of antenatal steroids in outcome

Discussion

Hyaline Membrane Disease (HMD) is a major cause of respiratory distress in preterm neonates, primarily due to pulmonary surfactant deficiency. Continuous Positive Airway Pressure (CPAP) is an effective non-invasive respiratory support method that can reduce the need for invasive ventilation. This present study aimed to evaluate the efficacy and outcomes of nasal CPAP in preterm neonates with HMD.

In our study, the incidence of prematurity was found to be 12.4%, which aligns closely with the national statistics of 10-12% in India [11]. In a similar study conducted by Parvathi et al., the reported incidence was 12.42% which is in concordance with our study findings.[1]

We observed that the incidence of Hyaline Membrane Disease (HMD) was 3.2%, notably higher than the 1.3% reported in the National Neonatal Perinatal Database (NNPD) 2002-03 report [10]. The study included 50 preterm neonates, with gestational ages ranging from 28 to 34 weeks, who were diagnosed with HMD and treated using early nasal CPAP. Of these 50 infants, 41 (82%) were successfully managed with nasal CPAP alone, while the remaining 9 (18%) required intubation and mechanical ventilation due to insufficient response to CPAP. In a similar study conducted by Parvathi et al., the outcomes of using nasal CPAP for treating Hyaline Membrane

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

Disease (HMD) in preterm neonates were reported. They observed an 80% success rate in managing the condition with nasal CPAP alone, while 20% of the infants failed to respond to the treatment and subsequently required more invasive mechanical ventilation. This was comparable to results of our study.[1]

Among the 9 infants who required mechanical ventilation, 88.9% were less than 32 weeks gestation, and only 11.1% were between 33 and 34 weeks. Statistical analysis demonstrated that outcomes improved significantly with increased gestational age, as evidenced by a p-value of less than 0.005. Similar findings were reported by Prashanth S et al., who noted better outcomes in neonates with a gestational age of less than 33 weeks, highlighting a substantial reduction in the requirement for mechanical ventilation from 76% to 35% (p=0.00001) [12]. Parvathi et al.,and Reddy et al also reported demonstrated that outcomes improved significantly with increased gestational age. This was in concurrence with our study[1,13]

Blood gas analysis was another critical factor used to determine the success or failure of early nasal CPAP treatment. Harris H et al. reported a marked improvement in mean PaO2 levels, rising from 47 to 80 mm Hg ($p<0.001$), with no significant alterations in PaCO2 or pH values. This finding underscores the effectiveness of CPAP in improving oxygenation [14].

A study by Boo NY et al. identified key predictors of CPAP failure in treating respiratory distress syndrome (RDS). Three significant risk factors associated with failed CPAP treatment were identified: moderate or severe RDS (odds ratio 5.9; 95% CI 1.5-50.7) and pneumothorax during CPAP therapy (odds ratio 6.9; 95% CI 1.1-41.7). In our study, 80% of the neonates who experienced CPAP failure presented with severe RDS [15].

A noteworthy finding from our study is the success rate of 93.1% in infants whose mothers received antenatal steroids, with a statistically significant p-value of less than 0.05. This result is consistent with findings by Sandri F et al., who observed a trend towards higher CPAP failure rates in neonates whose mothers had not received antenatal steroids (p=0.02) [16]. In a similar study by Parvathi et al. the reported success rate was 92.86% which was concurrent with our study.

Clinical Implications

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

The study highlights the efficacy of early nasal CPAP in managing HMD in preterm infants, with an 82% success rate in neonates treated exclusively with CPAP. These findings suggest that nasal CPAP can significantly reduce the need for invasive mechanical ventilation, thereby decreasing the associated risks and potential complications. The results also underscore the importance of gestational age as a determinant of CPAP success, as 88.9% of the neonates requiring mechanical ventilation were less than 32 weeks gestation, compared to only 11.1% aged between 33 to 34 weeks. This reinforces the need for stratified treatment approaches based on gestational age.

Blood gas analysis served as a critical parameter in determining the success or failure of early nasal CPAP. Additionally, the role of antenatal steroids was found to be pivotal, with a success rate of 93.1% in neonates whose mothers had received antenatal steroids, compared to those who had not. This reinforces the crucial role of antenatal steroids in enhancing lung maturity and improving CPAP outcomes in HMD.

Limitations

Despite its valuable findings, the study faced several limitations. The sample size of 50 neonates may not be sufficiently large to generalize the results across diverse populations. Additionally, the study was conducted at a single center, which may limit the applicability of the findings to other settings with different protocols and resources. The retrospective nature of part of the study may also introduce biases related to data collection and reporting.

Recommendations

Given the findings, several recommendations can be made to enhance the management of HMD in preterm neonates:

1. **Antenatal Steroid Administration:** Emphasis should be placed on the widespread administration of antenatal steroids to mothers at risk of preterm delivery, as they have been shown to significantly improve neonatal outcomes and CPAP success rates.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

2. **Early Intervention with Nasal CPAP:** Early initiation of nasal CPAP in neonates with HMD should be encouraged to reduce the need for invasive ventilation and associated complications.

3. **Gestational Age Considerations:** Treatment protocols should be stratified based on gestational age, with increased monitoring and potential early intervention for neonates under 32 weeks gestation, given their higher likelihood of requiring mechanical ventilation.

4. **Multicenter Studies:** Future research should involve multicenter studies with larger sample sizes to validate these findings across different populations and healthcare settings.

5. **Longitudinal Follow-Up:** Long-term follow-up of neonates treated with nasal CPAP would provide insights into potential developmental outcomes and further establish the efficacy of this approach.

Conclusion

In developing countries like ours, there is high burden of prematurity and sub-optimal use of antenatal steroid administration resulting infrequent HMD. In our study, we report that prematurity is the commonest predisposing factor for HMD. Its incidence increases as gestational age decreases. Early nasal CPAP is useful in mild and moderate grade HMD. Early nasal CPAP presents an effective, non-invasive option for managing mild to moderate HMD in preterm neonates It may not be a replacement for assisted respiratory support (ventilation) in severe HMD. Nasal CPAP is found to be effective in babies of mothers who had received antenatal steroids. Nasal CPAP is safe, inexpensive and effective means of respiratory support in HMD. Use of early nasal CPAP which is simple, non-invasive, has low capital outlay and does not require expertise, is the option for us where most places cannot provide invasive ventilation.

The study underscores the importance of gestational age and antenatal steroid administration in influencing CPAP outcomes, offering a promising avenue for reducing invasive ventilation needs, hospital stays, and neonatal complications. However, further research is warranted to

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

address the study's limitations and optimize treatment protocols for HMD across varied healthcare environments.

References

1. Parvathi et al. A Study on the use of Early Nasal Continuous Positive Airway Pressure (CPAP) in Preterm Neonates with Hyaline Membrane Disease (respiratory distress syndrome). JMSCR Volume 07 Issue 11 November 2019; 543-47.
2. Avery ME, Mead J. Surface properties in relation to atelectasis and hyaline membrane disease. AMA journal of diseases of children. 1959;97(5, Part 1):517-23.
3. Jobe A, Ikegami M, Jacobs H, Jones S, Conaway D. Permeability of premature lamb lungs to protein and the effect of surfactant on that permeability. J ApplPhysiol 1983; 55: 169-176.
4. Whitsett JA, Pryhuber GS, Rice WR, Warner BB, Wert SE. Acute respiratory disorders. In: Avery GB, Fletcher MA, MacDonald MG (eds), Neonatology: Pathophysiology and Management of the Newborn, 4 ed. Philadelphia: J.B. Lippincott Company; 1994: 429-452.
5. Chernick V. Continuous distending pressure in hyaline membrane disease: Devices, disadvantages and a daring study. Pediatrics 1973; 52: 114-15.
6. Harris TR, Wood BR. Physiologic Principles. In: Goldsmith JP,Karotkin EH eds. *Assisted Ventilation*, 3rd edn., Philadelphia; WB Saunders, 1996; 21-68.
7. Michna J, Jobe AH, Ikegami M. Positive end expiratory pressure preserves surfactant function in preterm lambs. Am J RespCrit Care Med 1999; 60: 634-639.
8. Lawson EE, Birdwell RL, Huang PS. Augmentation of pulmonary surfactant secretion by lung expansion at birth. Pediatr Res 1979; 13: 611-614.
9. Lee US, Dunn MS, Fenwick M et al. A comparison of underwater bubble continuous positive airway pressure (CPAP) with ventilator derived CPAP in preterm neonates ready for extubation. Biol Neonate 1998; 73: 69-75.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 09, 2024

10. Report of the National Neonatal Perinatal Database. National Neonatology Forum, India; 2002-03.

11. Meharban Singh. Care of the Newborn. 6th edn., page. 219.

12. Prashanth S Urs, Firdose Khan, Maiya PP. Bubble CPAP – A primary respiratory support for respiratory distress syndrome in newborns. Indian Pediatrics 2009; 46: 409-411.

13. Reddy RDMS, Koripadu S,Yanamandala HV.Use of early nasal continuous positive airway pressure in preterm neonates with hyaline membrane disease (neonatal respiratory distress syndrome). Int J Contemp Pediatr 2021;8:488-94.

14. Finer NN, Carlo WA, Walsh MC, Rich W, Gantz MG, Laptook AR, et al. Early CPAP versus surfactant in extremely preterm infants. The New England journal of medicine. 2010;362(21):1970-79

15. Boo NY, Zuraidah AL, Lim NL et al. Predictors of failure of nasal continuous positive airway pressure in treatment of preterm infants with respiratory distress syndrome. J Tropical Pediatr. 2000 Jun; 46(3): 1725.

16. Sandri F, Ancora G, Lanzoni A et al. Prophylactic nasal continuous positive airways pressure in newborns of 28-31 weeks gestations : multicenter randomized controlled clinical trial. Arch Dis Child Fetal Neonatal Ed. 2004 Sep; 89(5): F394- 8.