Original Article



Early Bubble Continuous Positive Airway Pressure Therapy for Premature Neonates with Respiratory Distress Syndrome

Jawaria Zia¹, Nahdia Zaman², Anam Zafar³, Hassan Mumtaz⁴, Sonia Fazal⁵

¹FCPS Pediatrics, Senior Registrar, HFH Rawalpindi, ²FCPS Pediatrics, Ex Senior Registrar, HFH Rawalpindi, ³FCPS Pediatrics, SMO, KRL Hospital Islamabad, ⁴Clinical Research Associate, Maroof International Hospital, Islamabad, ⁵FCPS Pediatrics, Senior Registrar HEH Rawalpindi

	rcrs rediatrics, senior Registrar HFH Rawaipindi
Author`s	A B S T R A C T
Contribution	Objective: To determine the outcome of preterm neonates with the early
¹ Conception of study/ Designing	introduction of bubble continuous positive airway pressure (CPAP).
/Planning, Manuscript writing	Methodology: This observational study was conducted in NICU of Shifa
^{2,3} Experimentation/Study	International Hospital, Islamabad from March 2017 to August 2017. Ninety
conduction, Critical review	preterm infants were enrolled with a gestational age of 28 to 37 weeks and with
^{4,5} Analysis/Interpretation,	the clinical features of Respiratory Distress Syndrome (RDS). Infant variables
Discussion, Facilitated for	that were recorded were birth weight, gestational age, and severity of RDS and
reagents/Material analysis	Fio2 requirement. Bubble CPAP was started at 5cm of water and FiO2 adjusted
Funding Source: None	to maintain SpO ₂ of 87 to 95%. The SPSS 26 version was used to analyze data.
Conflict of Interest: None	The Chi square test was used, with a P value of <0.05 considered significant.
Received: Nov 17, 2021	Results: The study included 90 neonates who were clinically diagnosed with
Accepted: Mar 15, 2022	RDS. To treat RDS, CPAP was started at the mean age of 5.27 hours of life with a
Address of Correspondent	standard deviation of 2.66 hours. 11 out of 90 (11.22%) babies had chest X-ray
Dr Nahdia Zaman	findings in favor of severe RDS; while X-rays of the remaining 79 (88.78%)
FCPS Pediatrics, Ex SR HFH	showed mild to moderate RDS.
Rawalpindi	Conclusion: CPAP is of valuable importance in low resource countries with a
nadi_zam21@yahoo.com	lack of ventilators and provides an adequate and conservative treatment
	method of mild to moderate RDS for preterm neonates. However, in cases of
	severe RDS, intubation and mechanical ventilation are often necessary.
	Keywords: Bubble continuous positive airway pressure, RDS, Preterm neonates,
	NICU.

Cite this article as: Zia J, Zaman N, Zafar A, Mumtaz H, Fazal S. Early Bubble Continuous Positive Airway Pressure Therapy for Premature Neonates with Respiratory Distress Syndrome. Ann Pak Inst Med Sci. 2021; 18(1):41-45. doi. 10.48036/apims.v18i1.582

Introduction

Preterm birth has become an epidemic globally, with 15 per million incidences.¹ The United Nations Sustainable Development Goal (SDG) 3.2 aims to 'end neonatal preventable deaths and under five-year-old children's by 2030, 'with all countries aiming to reduce their neonatal mortality rate to as low as 12 per 1,000 live births'.² Preterm birth is the leading cause of mortality in less than 5 years old and associated lengthy hospital stay increases morbidity.³ Among the low- and middle-income countries like Pakistan almost 12% of babies are born prematurely, with an estimated 99% of newborn deaths.⁴

Neonatal respiratory distress syndrome is an important cause of morbidity and mortality in premature neonates.⁵ In preterm babies who develop respiratory distress, the

early use of CPAP reduces respiratory failure, the need for mechanical ventilation, and decreased mortality⁶ in areas with low resource settings and limited infrastructure.

Studies in low resource countries show that due to financial restrictions, mortality in newborns is ten times higher than developed countries.⁷ so babies requiring mechanical ventilation cannot be referred. Around 50% preterm neonates develop RDS and use of early CPAP reduces the risk of mortality by around 48% along with a 50% reduction in the need for surfactant and mechanical ventilation.⁸ In such low resource setups bubble CPAP provides a safe and effective noninvasive means of respiratory support for a premature infant reducing RDS related mortality. It is a simple and less expensive method to deliver pressurized, humidified, and warm air to reduce

lung and alveolar collapse. With this technique a continuous and distending pressure is applied to the infant's airways (about 5 to 7cm of H₂O) which splints the alveoli open and obviates the need for mechanical ventilation. Trials done in developed countries and a Cochrane review showed that CPAP groups needed a few days on ventilation and had a significantly lower mortalityrate.⁹ Nowadzky et al and Klerk studies found the use of bubble CPAP a better practice as it decreased the need for mechanical ventilation and mortality.^{10,11} A study done in Malawi showed 64.5% of neonates with RDS requiring CPAP were discharged as compared to the 23% of the simple nasal oxygen receiving group. In a low resource academic NICU of South Africa not supporting infants with mechanical ventilation it was discovered that the majority of 69% of infants managed with CPAP alone and 80% survived to discharge. Another study by Koyamaibole found that the introduction of bubble CPAP reduced the need for mechanical ventilation by 50% and nurses can easily apply bubble CPAP after a month of training.¹² Studies from India also show the easy availability of bubble CPAP in low resources areas and it is associated with good results by using bubble CPAP. Initiating CPAP alone in all spontaneous breathing preterms with RDS surfactant and administration to only those on mechanical ventilation decreases the need for intubation and surfactant administration with no effect on the outcome.¹³

Continuous positive airway pressure (CPAP) in the form of bubbles may be useful in hospitals in low- and middleincome countries to improve pulmonary support. The purpose of this study is to find out if bubble CPAP can be used in Pakistani hospitals because they lack the ability to use ventilators. In order to prevent the morbidity and mortality caused by prematurity and RDS in newborns, nurses should be trained in the proper use of this equipment.

Methodology

This descriptive case series was conducted in the NICU of Shifa International Hospital for a period of six months from March 2017 to August 2017 after ethical approval. A sample size of 90 was calculated by WHO calculator, keeping an anticipated population proportion of 25%, absolute precision of 9%, and a confidence interval of 95%. A consecutive non-probability sampling technique was used.

Inclusion & Exclusion Criteria: Infants having gestational age of 28 to 37 weeks, admitted to the neonatal intensive care unit with the clinical features and chest x-ray suggestive of RDS were included in our study. Babies who require intubation at birth and those with congenital anomalies were excluded.

Data was collected after approval from the ethical committee and taking consent from parents. Preterm infants were started on bubble CPAP that was indigenously prepared by the NICU staff nurses. The gestational age calculation was based on the mothers last menstrual day or early pregnancy scan. Infant variables that were recorded were birth weight, gestational age, and severity of RDS and Fio2 requirement of infants on bubble CPAPPEEP was started at 5cm of water and FiO2 adjusted to maintain SpO2 of 87 to 95% and minimum flow was titrated to produce continuous bubbling in the CPAP circuit bottle. Bubble CPAP was considered to be failed if the FiO₂ requirement exceeded 50%, the baby had recurrent or prolonged apneas or cyanosis and poor perfusion. In the group who did not respond to CPAP the severity of RDS and FiO₂ requirements greater than 50% was noted. SPSS 26 version was used to analyze data.

Qualitative variables such as gender, CPAP failure FiO_2 and severe RDS was measured as frequency and percentages. Quantitative variables age, gestational age and birth weight was measured as mean±SD. Effect modifiers like age, gestational age, birth weight, gender, and antenatal steroids were controlled by stratification. For stratification chi square test was applied. P value < 0.05 was considered significant.

Results

The study included 90 neonates who were clinically diagnosed with RDS. All the neonates included in the study had a mean gestation period of 32.39 ± 2.69 weeks and mean birth weight of 1827.79 ± 532.97 grams. To treat RDS in these neonates, CPAP was started at the mean age of 5.27 hours of life with a standard deviation of 2.66 hours. Gender distribution in the sample set was 62 males (69.71%) to 28 females (30.29%), as shown in Table I.

While studying the intensity of RDS in these neonates, 11 out of 90 (11.22%) babies had chest X-ray findings in favor of severe RDS, while X-rays of the remaining 79 (88.78%) showed mild to moderate RDS.

Table 1: General charactedduring study.	eristics of stu	dy population	
	Me	Mean±SD	
Gestation Period (Weeks)	32	39±2.69	
Birth Weight (g)	1827.2	1827.79±532.97	
Age (h)	5.27	2.66	
Gender			
Males	68.89%	62/90	
Females	30.29%	28/90	

Nineteen out of 90 babies (20.21%) required FiO_2 more than 50%, while for the remaining 71 (79.79%), FiO_2 requirement was less than 50%. When the mothers of these neonates were studied, 84 out of 90 (94%) had received antenatal steroids. Overall, 10 (11%) babies from a total of 90 failed CPAP and of these 10 CPAP failure cases, 9 had severe RDS.

37 out of 41 (90.24%) infants were aged than 3 hours having successful CPAP whereas 43 out of 49 (87.75%) infants were aged more than 3 hours. 53 males out of 62(85.48%) had successful CPAP whereas 27 females out of 28 (96.42%) had successful CPAP. 9 males (14.52%) showed a higher likelihood of failing CPAP than females 3.58%, showing a significant p value. 73 out of 81 (90.12%) infants had a successful CPAP taking Antenatal steroids whereas 7 out of 9 (77.8%) had no steroids given. 47 out of 55 (85.45%) infants below the weight of 2000g had their CPAP successful Whereas only 33 out of 35 (94.28%) had successful CPAP at a birth weight of more than 2000g, showing a significant p value. 35 out of 43 (81.39%) infants having a gestational age less than 30 weeks had successful CPAP whereas 45 out of 47

 Table II: Stratification for CPAP Success w.r.t Age,

 Gender, Antenatal Steroid, Birth Weight & Gestational

 Age

Age Groups	Ν	CPAP Success		P-Value
- -		Yes	No	
< 3 Hours	41	37(90.24%)	4(9.76%)	0.28
> 3 Hours	49	43(87.75%)	6(12.25%)	
		Gender		
Male	62	53(85.48%)	9(14.52%)	0.000
Female	28	27(96.42%)	1(3.58%)	
		Antenatal Ster	oid	
Steroid Given	81	73(90.12%)	8(9.88%)	
No Steroid	9	7(77.8%)	2(22.2%)	0.033
Given				
		Birth Weigh	t	
< 2000g	55	47(85.45%)	8(14.55%)	
> 2000g	35	33(94.28%)	2(5.72%)	0.004
		Gestational A	ge	
< 30 weeks	43	35(81.39%)	8(18.60%)	0.01
> 30 weeks	47	45(95.74%)	2(4.26%)	

(95.74%) had successful CPAP having a gestational age more than 30 weeks, has significant p value 0.01 as shown in Table II.

Discussion

Study showed that CPAP is a highly effective modality for the treatment of RDS in preterm neonates with a success rate of around 90%, it surely holds the potential to be a routine treatment for premature infants with mild to moderate RDS.^{14, 15} However, it has limitations as well when it comes to extreme cases like neonates with very low birth weights, having severe RDS and requiring FiO₂> 50%. Still, considering the current infrastructure in developing countries like Pakistan lacking trained nursing staff, ventilators and neonatal intensive care units this simple and effective method can surely be of valuable use.^{16,17}

The CPAP was prepared by NICU staff so that PEEP was started at 5cm of water and FiO₂ was adjusted to maintain SpO₂ between 87 to 95% and minimum flow was titrated to produce continuous bubbling in the CPAP circuitbottle.¹⁸ In a study done by Dargaviolle predictors of failure of CPAP were identified, in their study about 22% of the infants applied CPAP failed and characteristically CPAP failure likelihood increased with lower gestational age. Most of the infants had severe RDS in the failure group, which was proven radiologically. Also, a high FiO₂ requirement more than 50% was associated with CPAP failure and adverse outcomes.¹²

In a study done in Iraq CPAP failure was associated with low gestational age i.e., age less than 30 weeks of gestation. In this study FiO₂ was noted at 20 minutes and those requiring more than 50% were found to be at a greater risk for failing CPAP. Most of the infants failing CPAP have a lower gestational age. Most of them had a high FiO₂ requirement >50% in first few hours of life and is associated with CPAP failure and adverse outcomes.¹³

In a study done by Saxena A et al in India, nasal CPAP was administered to all preterm neonates over a period of time. In this study, 83 babies were enrolled, of which the failure rate was 39.76%. 61.24% of the babies were managed on CPAP alone. The male to female ratio in this study was 2:1 which also like our study shows that male babies are more prone to developing RDS. So these two studies done in India in a relatively similar setup by Saxena et al and Mathai SS et al have comparatively similar results to our study so this can be employed in

NICU setups in Pakistan to improve the outcome of premature infants with RDS.¹⁹

In a study done by Koti et al 14% of the babies failed CPAP. The risk factors for CPAP failure were no exposure to antenatal steroids, White out CXR, sepsis/pneumonia, and $FiO_2 > 50\%$ after 15-20 minutes of CPAP. The median age of starting CPAP was 1.7 hrs. Of life in this study, mean gestational age was 30.98 ± 2 weeks while the mean birth weight was 1387 ± 402 grams. 91.1% mothers received antenatal steroids and 25% of the babies failed CPAP in Indian study. In our study, we did not evaluate for sepsis, but other factors such as FiO_2 requirement greater than 50% and white out CXR which means severe RDS are similar predisposing factors as seen in our study.²⁰

The biggest strength of our study is that it shows the outcomes of all the infants who were delivered or brought from another hospital in study period. Pakistan is a country where ventilator facilities for babies are very few and neonatal mortality is very high. Nurses can be taught to make this bubble CPAP and given training in order for many neonates with mild to moderate RDS to be treated without the need for mechanical ventilation, which is by far in short supply in comparison to the population we are dealing with.^{21,22}

Conclusion

It was concluded that CPAP is of valuable importance in low resource countries with a lack of ventilators and provides an adequate and conservative method of treatment of mild to moderate RDS for preterm neonates. However, in cases of severe RDS, intubation and mechanical ventilation are often necessary.

References

- Purisch SE, Bannerman CG. Epidemiology of preterm birth.Semin Perinatol,2017 ;41(7):387-391 <u>https://doi.org/10.1053/j.semperi.2017.07.009</u>
- United Nations. Transforming our world: the 2030 agenda for sustainable development 2015. A/RES/70/1. New York: United Nations.
- Lee A C, Blencowe H, Lawn J E. Small babies, big numbers: global estimates of preterm birth. The Lancet 2018; Volume 7(1) E2- E3, January 01,2019. <u>https://doi.org/10.1016/S2214-109X(18)30484-4</u>
- Ahmed M and Won Y. Cross-National Systematic Review of Neonatal Mortality and Postnatal Newborn Care: Special Focus on Pakistan. Int J Environ Res Public Health. 2017; 14(12): 1442. https://doi.org/10.3390/ijerph14121442

- De Luca D, Autilio C, Pezza L, et al. Personalised Medicine for the management of RDS in preterm neonates. NEONATOLOGY 2021;118:127-138 E PUB 2021. <u>https://doi.org/10.1159/000513783</u>
- Ho JJ, Subramaniam P, Davis PG, et al. Continuous positive airway pressure (CPAP) for respiratory distress in preterm infants. Cochrane Database Syst Rev.2020 Oct 15;10(10):CD002271. https://doi.org/10.1002/14651858.CD002271.pub3
- Dyer J. Neonatal Respiratory Distress syndrome: Tackling A Worldwide Problem. P T.2019; 44(1): 12-14
- Thukrai A, Sankar MJ, Chandrasekaran A, et al. Efficacy and safety of CPAP in low and middle income countries. Journal of Perinatology, 2016;36, S21-28 <u>https://doi.org/10.1038/jp.2016.29</u>
- Ho JJ, Subramaniam P, Henderson-Smart DJ, Davis PG. Continuous distending pressure for respiratory distress syndrome in preterm infants. Cochrane Database Syst Rev. 2015.

https://doi.org/10.1002/14651858.CD002271.pub2

- Nowadzky T, Pantoja A, Britton JR. Bubble continuous airway pressure, a potentially better practice reduces the use of mechanical ventilation among very low birth weight infants with respiratory distress syndrome. Pediatrics.2009;123:1534-40 https://doi.org/10.1542/peds.2008-1279
- 11. DeKlerk, De KlerkRK. Nasal continuous positive airway pressure and outcomes of preterm infants. J Paed chi.2001;37:161-7 https://doi.org/10.1046/j.1440-1754.2001.00624.x
- 12. Dargaville PA, Aiyappan A, De Paoli AG, Dalton RG, Kuschel CA, Kamlin CO et al. Continuous positive airway pressure failure in preterm infants: incidence, predictors and consequences. Neonatology. 2013; 104:8-4. https://doi.org/10.1159/000346460
- Hameed NN, Abdul Jaleel RK, Saugstad OD. The use of continuous positive airway pressure in preterm babies with respiratory distress syndrome: a report from Baghdad, Iraq.J Matern Fetal Neonatal Med. 2014; 27(6):629-32. <u>https://doi.org/10.3109/14767058.2013.825595</u>
- Mathai SS, Rajeev A, AdhikariKM.Safety and effectiveness of bubble continuous positive airway pressure in preterm neonates with respiratory distress. Med J Armed Forces India.2014; 70:327-31. https://doi.org/10.1016/i.miafi.2013.08.003
- 15. Ghafoor T, Mahmud S, Ali S, Dogar SA; Incidence of Respiratory Distress Syndrome. J CollSurg Pak 2003;13:271-273
- Bhutta ZA, Yusuf K, Khan IA, Is Management of Neonatal Respiratory Distress Syndrome feasible in developing countries? Experience from Karachi (Pakistan). Pediatric Pulmonology 1999;27:305-311 <u>https://doi.org/10.1002/(SICI)1099-</u> 0496(199905)27:5<305::AID-PPUL2>3.0.CO;2-Q
- Pinto VL, Sharma S. Continuous positive airway pressure. {Updated 2021 Jul31}. In: StatPearls(Internet). Treasure Island (FL):Stat Pearls Publishing;2022 Jan.

- Kondwani Kawaza, Heather E. Machen, Jocelyn Brown, Zondiwe Mwanza, Suzanne Iniguez, Al Gest, E. et al. Efficacy of a Low-Cost Bubble CPAP System in Treatment of Respiratory Distress in a Neonatal Ward in Malawi. PLoS One. 2014; 9(1): e86327. <u>https://doi.org/10.1371/journal.pone.0086327</u>
- Saxena A, Thapar RK, Sondi Chandra. Continuous Positive airway pressure for spontaneously breathing premature infants with respiratory distress syndrome. Indian J Pediatr.2012; 79:1185-91. <u>https://doi.org/10.1007/s12098-012-0722-z</u>
- Koti J, Murki S, Gaddam P, Reddy A, Reddy MD. Bubble CPAP for respiratory distress syndrome in preterm infants.Indian Pediatr.2010;47:139-43 https://doi.org/10.1007/s13312-010-0021-6
- 21. Kirsten GF, Kirsten CL, Henning PA, et al. The outcome of ELBW infants treated with NCPAP and InSurE in a resource limited institution. Pediatrics.2012;129(4)952-59 https://doi.org/10.1542/peds.2011-1365
- 22. Koyamaibole L, Kado J, Qovu JD, Colquhoun S, Duke T. An evaluation of bubble-CPAP in a neonatal unit in a developing country: effective respiratory support that can be applied by nurses. J Trop Pediatr. 2006;52(4):249–53 <u>https://doi.org/10.1093/tropej/fmi109</u>