Original Article **Open Access**

Use of Non-Invasive Ventilation in Reducing Partial Pressure of Carbon Dioxide Level ($PaCO_2$) in Neonates with Respiratory Distress Syndrome

Rida Ali, Shahid Mahmud

ABSTRACT:

Objective: It has been observed that non-invasive ventilation used in premature with Respiratory distress syndrome and notably decrease level of partial pressure of carbon-dioxide ($PaCO_2$) level in blood. The primary goal of this study was to assess the effect of non-invasive ventilation in decreasing the level of partial pressure of carbon dioxide ($PaCO_2$) level and supplementary oxygen need in premature neonates with RDS.

Study Design and Settings: This randomized controlled trial was done in Jan 2021 till August 2021 at PNS SHIFA Karachi.

Methodology: Neonates with gestational age (GA <34 wk) with RDS at birth were randomly assigned to nasal intermittent positive pressure ventilation (NIPPV) and nasal high frequency oscillatory ventilation (NHFOV) for respiratory support after giving surfactant .Twenty three preterm babies were included in each group .Level of partial pressure of carbon dioxide at 2hrs and 24hrs of non-invasive ventilation and supplementary oxygen need was evaluated.

Results: Non-invasive ventilation was found to reduce the $PaCO_2$ level (p= .01), NIPPV (43.06±13.74) vs. (33.63±19.99) in NHFOV at 2hrs and 24hrs NIPPV (19.89±7.18) vs. NHFOV (14.04±8.39).Value of pH was also significant in two groups with optimal mean airway pressure. Supplementary oxygen period were also reduced in NHFOV than NIPPV group (35.7% vs. 64.3%).

Conclusion: NHFOV was a beneficial mode in maintaining level of pH, $PaCO_2$ level and reducing need of supplementary oxygen in preterm babies with RDS.

Keywords: Intermittent Positive-Pressure Ventilation, Respiratory distress syndrome, high-frequency ventilation

How to cite this Article:
Ali R, Mahmud S. Use of Non-Invasive Ventilation in Reducing Partial Pressure of Carbon Dioxide Level (Paco2) in Neonates with Respiratory Distress Syndrome. J Bahria Uni Med Dental Coll. 2022; 11(3):148-151 DOI: https://doi.org/10.51985/JBUMDC2021106

INTRODUCTION:

In neonates transition of pulmonary mechanism just after birth leads to respiratory distress in 7% of preterm babies.[1] There are many causes of respiratory distress, surfactant deficiency is one of the commonest cause of Respiratory distress syndrome among preterm neonates. The immaturity of lungs causes respiratory failure, that leads to decrease in the partial pressure of oxygen (PaO_2) with increment in the partial pressure of carbon-dioxide ($PaCO_2$).[2] The in-sufficiency of lungs cause various morbidities as well as mortality in premature neonates. Mechanical ventilation is the novel respiratory strategy in providing respiratory support. Prolonged use of invasive mechanical ventilation is associated with various ventilator induced complications like volutrauma, chronic lung disease, pneumothorax and bronchopulmunary dysplasia and other morbidity in premature neonates. This has been shown many times, that chronic lung injury can be decreased by reducing time of invasive ventilation. New mode of non–invasive respiratory modes nasal High Frequency Oscillatory Ventilation (NHFOV), Nasal Intermittent Positive Pressure Ventilation (NIPPV), nasal continuous positive airway pressure (NCPAP), are undergoing at present in China to see the trends of respiratory support.[3] A survey has been conducted in European countries which showed that 17% use of nasal HFOV in contrast to NCPAP, in less than 1500 gms premature neonates when nasal CPAP was failed, but it needs time to accept this new strategy.[4]

Nasal High Frequency Oscillatory Ventilation (NHFOV) is superior to other non-invasive ventilation technique in preventing respiratory failure in premature in previous two retrospective studies.[5] Nasal intermittent positive pressure ventilation enhances continuous positive airway pressure along with additional lung inflation at preset peek pressure (15-22 cmH2o), that improves tidal and minute volume with reduced inspiration capacity ,to maintain thoracic wall movement in newborns for better lung compliance.[6]

Rida Ali
Assistant Professor, Paediatrics
PNS SHIFA / Bahria University Medical & Dental College
Email: drrida.ali09@gmail.com

Shahid Mahmud
Head of Department Paediatrics & Neonatal Medicine.
PNS SHIFA / Bahria University Medical & Dental College
Email: childspec@hotmail.com

Received: 17-Nov-2021
Accepted: 16-Jun-2022

Nasal High Frequency Oscillatory Ventilation does not need synchronization and increases rate of carbon-dioxide clearance. There are two justifications for nasal high frequency oscillatory ventilation (NHFOV) in clearance of carbon-dioxide level. The combined features of invasive high frequency oscillations with add-on nasal CPAP is effective in improving lung ventilation by low air trapping in lungs ,even at high pressure and adequate glottis expansion through continuous oscillation, that cause increase CO_2 removal from the lungs.[7] In addition ,laryngeal constriction and distention in abdomen is limited that assists in aeration of lung.[8] On the other end, nasal CPAP is not effective in reducing CO2 successfully due to ineffective oscillation.[9]

Few studies have been done using nasal HFOV and NIPPV mode as a primary respiratory mode. This is the first study to our knowledge that is done in Pakistan using this respiratory support as primarily in neonates .The main objective of this study was to assess the efficacy of non-invasive ventilation as a primary respiratory support, in decreasing the level of partial pressure of carbon-dioxide level ($PaCO_2$) and need of supplementary oxygen ,in premature neonates with respiratory distress syndrome. Our hypothesis was nasal high frequency ventilation will be effective in reducing level of $PaCO_2$ level and decreasing the need of supplementary oxygen.

METHODOLOGY:

A randomized controlled trial was done from March 2021 to Aug 2021 at neonatal unit PNS SHIFA Hospital Karachi. According to Helsinki Declaration, Consent from Ethical review committee was taken (ERC/2021/PED/52), informed consent and permission for publication was taken from parents. Neonates with GA less than 34 wk with clinical signs of respiratory distress syndrome as tachypnea, grunting and nasal flaring were enrolled. Neonates with any pulmonary leak, congenital pneumonia, congenital cardiac defect, cardiopulmonary resuscitation, congenital diaphragmatic hernia, intraventricular bleed, and pulmonary hemorrhage were not enrolled. Open Epi Version 3 software was used for sample size, at 95% confidence interval with 5% margin error. By taking reference study,[10] sample size was taken 23 in each group (NHFOV vs. NIPPV) with total of 46.Neonates with clinical signs of respiratory distress syndrome at birth were randomly given NHFOV and NIPPV with sealed opaque envelopes. Nasal high frequency oscillation (MEDIN Germany) given by nasal mask as per size of nares, settings were frequency 8 (range 8-10) and amplitude 7 (7-10) MAP 6cmH_2O (6-10),non-invasive positive pressure ventilation (CNO-MEDIN Germany) PEEP 6,PIP 15, Rate 45 (40-50),IT 0.40 sec, FiO_2 was maintained to keep SpO_2 90-94% >30wk and 89-93% <30wk.[11] Neonates were given injection Curocef with dose of 2.5 ml per kg with INSURE method followed by second dose of 1.5ml per kg if FiO_2 >40% to keep SpO_2 90-94% in >30 wk and 89-93% in <30 wk before allocation of respiratory support. Patients were weaned off from respiratory support once fiO_2 < 0.25%, MAP < 6 and no sign of respiratory distress. Injection Caffeine 20 mg/ kg loading followed by 10 mg/kg once a day, was given for preterm babies with apnea. Neonates were immediately kept on mechanical ventilator, if hypoxia with severe respiratory distress develop, respiratory acidosis $PaCO_2$ >65 and pH <7.2, apnea with bradycardia and need of cardiopulmonary resuscitation[12,13].

Patient's general characteristics were recorded in a structured Performa by researcher that included, birth weight, gestational age, gender, mode of delivery, antenatal corticosteroid, premature rupture of membrane, signs of RDS.

Primary outcome were decreased level of $PaCO_2$ after 2 hrs and at 24 hrs were checked by (taking capillary blood sample) arterial blood gas machine portable at incubator side. Period of non-invasive ventilation and need of supplementary oxygen in two group's nasal HFOV and NIPPV in preterm with RDS during the admission stay of hospital.

Data analysis was done by SPSS version 19 .Student's *t*-test was applied for continuous data. Chi-squared test was applied for comparison of proportions, student's t-test for continuous data and Fisher's exact test for categorical data. $P < 0.05$ was considered as statistically significant.

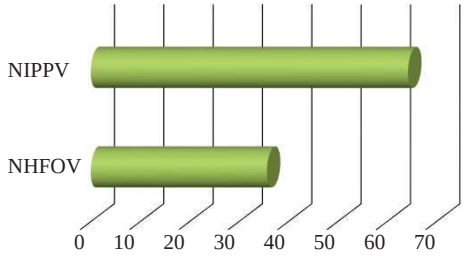
RESULTS:

46 neonates (23 in each group) were enrolled in March 2021 to August 2021 and randomly divided to nasal HFOV and NIPPV group. There was no difference found in the general characteristics of neonates in two groups .The mean Gestational age in weeks (nasal HFOV 29.96±2.38vs NIPPV 43.58±61.03),weight in grams (nasal HFOV 1347±458 vs. NIPPV 1672±534) , male / female ratio (NHFOV 13/11 vs. NIPPV 16 /8), delivered via LSCS nasal HFOV (42.1%) and NIPPV (57.9%) and antenatal corticosteroids were given to (NHFOV 51.1% vs.NIPPV48.9%).Value of pH was stable in NHFOV group (p=.04) at 2 hours and (p=.02) at 24 hours.$PaCO_2$ and HCO_3 was decreased significantly in nasal HFOV than NIPPV group as shown in Table 1.Whereas need of supplementary oxygen in NHFOV was (p=.01) as shown in Fig 1.No difference was found in period of non-invasive ventilation . Mean airway pressure (nasal HFOV 5.72± 0.17 & NIPPV 5.71 ± 0.26 p = 0.44).

Table 1: Outcome Variables

Variables	NHFOV(n=23)	NIPPV(n=23)	p-value
At 2hours			
$PaCO_2$	33.63±19.99	43.06±13.74	.063
HCO3	15.41±8.02	19.82±4.04	.020
At 24 hours			
$PaCO_2$	14.04±8.39	19.89±7.18	.013
HCO3	14.04±8.39	19.89±7.18	.013

Figure 1: Period of Oxygen Supplimentation



DISCUSSION:

Nasal high frequency ventilation was found to be effective in reducing need of invasive mechanical ventilation.[14] Nasal high frequency ventilation was a new respiratory strategy in eliminating CO2.In a retrospective study by Mukerji, showed that nasal HFOV used as an extubation mode in contrast to nasal CPAP in eliminating carbon-dioxide level, decrease apnea episodes, bradycardia and desaturation.[15] Where as, in a randomized crossover trial by Rüegger et al, carbon-dioxide level was not maintained besides premature neonates were given nasal HFOV at 4 hours after giving surfactant.[16]

We applied nasal high frequency oscillatory ventilation as a primary respiratory support, via nasal mask as interface. Our study showed, significant decline in $PaCO_2$ level in nasal HFOV (33.63±19.99) vs. NIPPV (43.06±13.74) after two hours and at 24 hours (14.04±8.39) vs. NIPPV (19.89±7.18), (p =.01) in neonates with GA 27 wk - 34 wk with respiratory distress syndrome. This pattern of lowering CO2 (46.6 ± 7.5 mmHg) on non-invasive high frequency ventilation was also noted in 206 neonates with GA <37wk with RDS after extubation at 6 hours and reduced need of re-intubation ,in a randomized controlled trial by Chen L in 2019.[17] Similar to our study ,Bottino R et al in randomized controlled trial 2018 ,studied that neonates with GA 26.4 ± 1.8 wk and birth weight 921 ± 177 gms , there was decreased partial pressure of carbon-dioxide ($PaCO_2$) in nasal HFOV (49.6 ± 8.7 vs. 56.9 ± 9.9) than nasal CPAP.[18]

In contrast to our study,Colaizy[19]also found reduced level of carbon-dioxide to 45 torr from 50 torr (p=.01) after 2 hours of nasal HFOV in relative similar gestational age of 26-30 wk neonates .Value of pH was also increased 7.40 after two hours of nasal HFOV. In another randomized controlled trial by Wu HL was conducted in 2021 in which infant with cardiac defects at birth ,had low threshold for post extubation respiratory failure post operatively ,as nasal HFOV was contrast reduced $PaCO_2$ in next 12 hours (43.6 ± 7.3 mmHg, p = 0.05)[20], a similar pattern as in our study .In comparison to our study, Danial did not find any difference in elimination of carbon-dioxide level at 4 hours of nasal high frequency oscillatory ventilation than NCPAP in 27 ±2 wk premature neonates,[21] whereas we have found decreased $PaCO_2$ level in nasal HFOV (33.63±19.99) vs. NIPPV (43.06±13.74) after two hours.

Mean airway pressure was remain constant in (nasal HFOV 5.72±0.17 vs. 5.71±0.26 NIPPV) in two groups of our study, in contrast (10.9 ± 2.06) to other previous studies[22].Our study did not show any major difference in the duration of non-invasive ventilation among preterm neonates, however oxygen supplementation was significantly low in nasal HFOV 35.7% than NIPPV 64.3% ,(p= .019).In contrast to NCPAP ,Malakianet al ,was shown contrast difference in duration of non-invasive ventilation in nasal HFOV (p=0.01) among 28 wk till 34 wk GA neonates,[23] whereas no difference in need of mechanical ventilation .Li Y et al stated that nasal HFOV was seen effective in decreasing non-invasive ventilation period, in preterm with GA <34 wk as an extubation respiratory support.[24] Zhu et al also studied the same GA 28WK-34wk as we did in our study ,for nasal HFOV and NCPAP as an initial respiratory support ,mechanical ventilation need was(p<0.01),hence period of non-invasive ventilation was not elicted.[10] It was seen in our study that oxygen supplementation was significantly decreased in nasal HFOV 35.7% than NIPPV 64.3%. Whereasa comparative study by Dursan 2019, using NIPPV vs. nasal CPAP ,didn't show any change in period of oxygen supplements but difference in endotracheal intubation need (p<0.05) in 24wk-32wk neonates.[25]

Nasal HFOV has been used as primordial non invasive respiratory support that was found to reduce the invasive mechanical ventilation need in premature neonate .It has been noted that nasal high frequency ventilation was used as an extubation mode in previous retrospective studies. Whereas in our study nasal high frequency oscillatory ventilation was used as a primary respiratory support in preterm neonates, very few studies in the past use this nasal HFOV as primary respiratory mode. Hence nasal high frequency ventilation was found to be effective respiratory derive in elimination $PaCO_2$, decreasing need of prolong ventilation add on shortening of supplementary oxygen support, besides period of non-invasive ventilation was not found significant in two groups of our study. A beneficial effect of decrease need of oxygen supplements in our study 35.7% as compared to NIPPV 64.3%, that prevent development of bronchopulmunary dysplasia in GA 27-34wk. High frequency ventilation has many aspects that are under observation. In this study we used nasal mask as an interface to deliver nasal HFOV which had been studied in past, but in our study it was effective in reducing $PaCO_2$ and supplementary oxygen requirement.

CONCLUSION:

Nasal high frequency oscillatory ventilation was significantly effective in reducing $PaCO_2$ level and supplementary oxygen demand among preterm with respiratory distress syndrome, that prevents an untoward effects of prolong mechanical ventilation.

Authors Contribution:
Rida Ali: Study Design, Data Collection, Write up
Shahid Mahmud: Literature Review

REFERENCES:

1. Agarwal R, Deorari A, Paul V, Sankar MJ, Sachdeva A. AIIMS Protocols in Neonatology. 2. Delhi: Noble Vision; 2019.
2. Shao XM, Ye HM, Qiu X. Practice of neonatology. People's Medical Publishing House. 2011:115-89.
3. Shi Y, De Luca D, Continuous positive airway pressure (CPAP) vs noninvasive positive pressure ventilation (NIPPV) vs noninvasive high frequency oscillation ventilation (NHFOV) as post-extubation support in preterm neonates: protocol for an assessor-blinded, multicenter, randomized controlled trial. NASalOscillatioN post-Extubation (NASONE) study group.BMCPediatr. 2019; 19(1):256. DOI: 10.1186/s12887-019-1625-1 d
4. Fischer HS, Bohlin K, Bührer C, Schmalisch G, Cremer M, Reiss I et al ,Nasal high-frequency oscillation ventilation in neonates: a survey in five European countries. Eur J Pediatr. 2015;174(4):465-71. DOI: 10.1007/s00431-014-2419-y
5. Wang CH, Shi LP, Ma XL, Lin HJ, Xu YP, Du LZ et al . Use of noninvasive high-frequency oscillatory ventilation in very low birth weight infants].2017; 55(3):177-181.DOI: 10.3760/cma.j.issn.0578-1310.2017.03.003
6. Owen LS, Morley CJ, Davis PG. Nasal intermittent positive pressure ventilation: what do we know in 2007?.Archives of Disease in Childhood. Fetal and Neonatal Edition 2007;92(5):F414-8.DOI: 10.1136/adc.2007.117614
7. Klotz D, Schaefer C, Stavropoulou D, Fuchs H, Schumann S. Leakage in nasal high-frequency oscillatory ventilation improves carbon dioxide clearance-A bench study. PediatrPulmonol. 2017; 52(3):367-372.DOI: 10.1002/ ppul.23 534
8. De Luca D, Piastra M, Pietrini D, Conti G .Effect of amplitude and inspiratory time in a bench model of non-invasive HFOV through nasal prongs. PediatrPulmonol. 2012; 47(10):1012-8. DOI: 10.1002/ppul.22511
9. DiblasiRM .Nasal continuous positive airway pressure (CPAP) for the respiratory care of the newborn infant. .Respir Care. 2009; 54(9):1209-35. PMID: 19712498.
10. Zhu XW, Zhao JN, Tang SF, Yan J, Shi Y .Noninvasive high-frequency oscillatory ventilation versus nasal continuous positive airway pressure in preterm infants with moderate-severe respiratory distress syndrome: A preliminary report..PediatrPulmonol. 2017; 52(8):1038-1042.DOI: 10.1002/ppul.23755
11. Cayabyab R, Arora V, Wertheimer F, Durand M, Ramanathan R. Graded oxygen saturation targets and retinopathy of prematurity in extremely preterm infants. Pediatr Res. 2016; 80(3): 401–406.DOI: 10.1038/pr.2016.98
12. Lista G, Castoldi F, Fontana P, Daniele I, Cavigioli F, Rossi S et al. Nasal continuous positive airway pressure (CPAP) versus bi-level nasal CPAP in preterm babies with respiratory distress syndrome: a randomised control trial. Arch Dis Child Fetal Neonatal Ed. 2010;95(2):F85–F89.DOI: 10.1136/adc.2009.169219
13. O'Brien K, Campell C, Brown L, Wenger L, Shah L. Infant flow biphasic nasal continuous positive airway pressure (BP-NCPAP) vs. infant flow NCPAP for the facilitation of extubation in infants = 1,250 grams: a randomized controlled trial. BMC Pediatr. 2012;12:43–51. DOI: 10.1186/1471-2431-12-43
14. Li J, Li X, Huang X, Zhang Z ,Noninvasive high-frequency oscillatory ventilation as respiratory support in preterm infants: a meta-analysis of randomized controlled trials. Respir Res. 2019; 20(1):58.DOI: 10.1186/s12931-019-1023-0
15. HaidarShehadeh ,Non-invasive high flow oscillatory ventilation in comparison with nasal continuous positive pressure ventilation for respiratory distress syndrome, a literature review. AM J Matern Fetal Neonatal Med. 2021; 34(17):2900-2909. DOI: 10.1080/14767058.2019.1671332
16. Mukerji A, Singh B, Helou SE, Fusch C, Dunn M, Belik J et al , Use of noninvasive high-frequency ventilation in the neonatal intensive care unit: a retrospective review. Am J Perinatol. 2015; 30(2):171-6.DOI: 10.1055/s-0034-1381317
17. Rüegger CM, Lorenz L, Kamlin COF, Manley BJ, Owen LS, Bassler D et al , The Effect of Noninvasive High-Frequency Oscillatory Ventilation on Desaturations and Bradycardia in Very Preterm Infants: A Randomized Crossover Trial.JPediatr. 2018; 201():269-273.e2. DOI: 10.1016/j.jpeds.2018.05.029
18. Bottino R, Pontiggia F, Ricci C, Gambacorta A, Paladini A, Chijenas V et al. Nasal high-frequency oscillatory ventilation and CO2 removal: A randomized controlled crossover trial. PediatrPulmonol. 2018; 53(9):1245-1251.DOI: 10.1002/ppul.24120
19. Colaizy TT, Younis UM, Bell EF, Klein ,Nasal high-frequency ventilation for premature infants. JM ActaPaediatr. 2008; 97(11):1518-22.DOI: 10.1111/j.1651-2227.2008.00900.x
20. Wu HL, Lei YQ, Xie WP, Chen Q, Zheng YR. Nasal High-Frequency Oscillatory Ventilation vs. Nasal Continuous Positive Airway Pressure as Therapy for Postextubation Respiratory Failure in Infants After Congenital Heart Surgery. Front Pediatr. 2021;9:700632.DOI: 10.3389/fped.2021.700632
21. Klotz D, Schneider H, Schumann S, Mayer B, Fuchs H . Non-invasive high-frequency oscillatory ventilation in preterm infants: a randomised controlled cross-over trial. Arch Dis Child Fetal Neonatal Ed. 2018; 103(4):F1-F5.DOI: 10.1136/archdischild-2017-313190
22. Seth S, Saha B, Saha AK, Mukherjee S, Hazra A. Nasal HFOV versus nasal IPPV as a post-extubation respiratory support in preterm infants-a randomised controlled trial. Eur J Pediatr. 2021;180(10):3151-3160. DOI: 10.1007/s00431-021-04084-1
23. Malakian A, Bashirnezhadkhabaz S, Aramesh MR, DehdashtianM .Noninvasive high-frequency oscillatory ventilation versus nasal continuous positive airway pressure in preterm infants with respiratory distress syndrome: a randomized controlled trial. J Matern Fetal Neonatal Med. 2020; 33(15): 2601-07. DOI: 10.1080/14767058.2018.1555810
24. Li Y, Wei Q, Zhao D, Mo Y, Yao L, Li L et al. Non-invasive high-frequency oscillatory ventilation in preterm infants after extubation: a randomized, controlled trial. J Int Med Res. 2021;49(2):300060520984915.DOI: 10.1177/ 03000605 2098 4915
25. Dursun M, Uslu S, Bulbul A, Celik M, Zubarioglu U, Bas EK. Comparison of Early Nasal Intermittent Positive Pressure Ventilation and Nasal Continuous Positive Airway Pressure in Preterm Infants with Respiratory Distress Syndrome. J Trop Pediatr. 2019;65(4):352-360. DOI: 10.1093/tropej/fmy058