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Efficacy of Nasal Continuous Positive Airway Pressure Versus Heated Humidified High-Flow Nasal Cannula as a Primary Mode of Respiratory Support in Preterm Infants with RDS

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Author`s Contribution

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ABSTRACT

Objective: To determine the efficacy of nasal continuous positive airway pressure (NCPAP) versus heated humidified high-flow nasal cannula (HHHFNC) as a primary mode of respiratory support in preterm infants with respiratory distress.

Methodology: This randomized controlled trial study was conducted at in patient department of neonatology (Nursery & NICU) of Pakistan Insitute of Medical Sciences (PIMS) from July 2020 to Dec 2020. A total of 280 neonates randomly divided (140 in each study group) of both genders, with gestational age between 28-34 weeks and having mild-to-moderate respiratory distress within 1st 6 hours of birth requiring non-invasive ventilation were enrolled. Neonates in NCPAP Group (n=140) were given NCPAP whereas neonates in HHHFNC Group (n=140) were given HHHFNC. The efficacy of both groups were compared on the basis of treatment failure within 1st 3 days, total duration (hours) of non-invasive ventilator (NIV) required and total duration (hours) of supplementary oxygen required.

Results: Overall, mean gestational age was noted to be 30.0+6.4 weeks. There were 144 (51.4%) neonates with birth weight between 1 to 1.4 kg, 90 (32.1%) between 1.5 to 1.9 kg and 46 (16.4%0 between 2.0 to 2.4 kg. Treatment failure was noted in 67 (47.6%) neonates in NCAP group while HHHFNC group reported 73 (52.4%) neonates with treatment failure (p=0.4733). No significant difference was observed in mean total duration of NIV support required (p=0.2598) or mean total duration of supplementary oxygen (p=0.1946) in between study groups.

Conclusion: HHHFNC had similar efficacy when compared to NCPAP among neonates with RDS. In comparison to NCPAP, HHHFNC could be a simple, well-tolerated and effective alternative in terms of respiratory support. No major difference in terms of complication was observed between both treatment approaches.

Keywords: Respiratory distress syndrome, Respiratory support, Nasal continuous positive airway pressure, heated humidified high-flow nasal cannula.

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Introduction

Prematurity is the leading cause of deaths in newborns worldwide.[1,2] Prematurity or preterm babies are those who are born alive before 37 weeks of gestation completed.2 Annually about 15 million preterm infants are born. Around 1 million of preterm babies (infants) die in neonatal period age due to respiratory complications.[3] According to UNICEF statistics has been on rise, and

around estimation 750,000 premature births recorded annually in Pakistan, out of which, around 50% survive.[4]

Respiratory complications are amongst the most common and severe complications in preterm neonates.[5] Respiratory distress syndrome (RDS) is considered to be the most frequent reason of respiratory distress in preterm newborns.[6] RDS is caused by the quantitative or qualitative deficiency of surfactant which is produced by type II Pneumocytes lining the alveoli. Preterm infants with RDS present immediately or soon after birth with difficulty in breathing or worsening respiratory distress. The clinical sign of RDS in preterm infant are tachyepnia, intercostal recession, subcostal recession, expiratory grunting, cyanosis and decreased breath sounds on auscultations.[7] RDS if untreated may lead to increasing fatigue, Apnea, hypoxia and can progress to respiratory failure.[8]

Preterm babies require assisted ventilator support (Noninvasive Ventilatroy Support) for the management of RDS. "Nasal continuous positive airway pressure (NCPAP)" is one of the simpler and effective approaches in newborns with RDS. It establishes and maintains lung functions by improving functional residual capacity, which leads to decreased work of breathing and other sign of respiratory distress. On the other hand, "Heated humidified high-flow nasal cannula therapy (HHHFNC)" is another popular non-invasive respiratory support for preterm infants.[9] Evidence confirms that HHHFNC is linked with reduction in respiratory distress, improves ventilation while decreasing the intubation in infants with RDS.[10] The aim is to treat hypoxia and hypercarbia associated with RDS by non-invasive respiratory support. This study was done to determine the efficacy of NCPAP and HHHFNC as a primary mode of respiratory support in preterm infants with RDS.

Methodology

It was a randomized control trial was conducted at In-patient department of neonatology (Nursery & NICU) of Pakistan Institute of Medical Sciences (PIMS) of Shaheed Zulifqar Ali Bhutto Medical University from July, 2020 to Dec, 2020. Approval from institutional ethical committee was taken. Written consent was sought from parents/guardians of all study participants. A total of 280 neonates (140 in each study group) of both genders, with gestational age between 28-34 weeks and having mild-to-moderate respiratory distress within 1st 6 hours of birth requiring non-invasive ventilation were enrolled. Respiratory distress was labeled on the basis of clinical and laboratory criteria. Clinical criteria included presence of following signs in 1st 6 hours of life; tachypenia (respiratory rate > 60 breaths per min), grunting, moaning, lower chest indrawing and nasal flaring. Laboratory criteria included ABGs with carbon dioxide > 50 mmHg. All neonates born with Apgar score < 5 at 5 minutes or those having any nasopharyngeal pathology / associated surgical illness (e.g. cleft lip, cleft palate, or choanal atresia) or having congenital heart disease were excluded.

Neonates admitted in nursery & NICU were included. Neonates were randomly divided into two equal groups. Neonates in NCPAP Group (n=140) were given NCPAP whereas neonates in HHHFNC Group (n=140) were given HHHFNC. The efficacy of both groups were compared on the basis of treatment failure within 1st 3 days, total duration (hours) of non-invasive ventilator (NIV) required and total duration (hours) of supplementary oxygen required. Data of all neonates was collected on a structured proforma.

Data was entered and analyzed in SPSS version 26.0. Mean and standard deviation (SD) were calculated for quantitative variables like age, 'total duration (in hours) of non-invasive ventilation NIV support 'and 'total duration (in hours) of supplemental oxygen' requirement. Qualitative variables like gender was expressed as frequencies and percentages. Independent sample t-test was used to compare non-invasive ventilation (NIV) and total duration (hrs) of supplemental oxygen requirement among both the groups while chi square test was used to compare gender distribution between both study groups. P-value < 0.05 was considered as significant.

Results

In a total of 280 neonates, 154 (55.0%) were female. Overall, mean gestational age was noted to be 30.0±6.4 weeks. There were 144 (51.4%) neonates with birth weight between 1 to 1.4 kg, 90 (32.1%) between 1.5 to 1.9 kg and 46 (16.4%0 between 2.0 to 2.4 kg. Antenatal administration of dexamethasone to mothers for RDS prevention was noted among 34 (12.1%) mothers. (Table) I is showing comparison of characteristics of neonates between both study groups and no statistically significant difference was noted (p>0.05).

Treatment failure was noted in 67 (47.6%) neonates in NCAP group while HHHFNC group reported 73 (52.4%) neonates with treatment failure (p=0.4733). Mean total

duration of NIV support required was observed to be 219.1±68.7 hours in NCAP group versus 228.8±74.9 hours in HHHFNC group (p=0.2598). Mean total duration of supplementary oxygen was observed to be 28.4±4.3 hours in NCAP group versus 29.1±4.7 hours in HHHFNC group (p=0.1946). Table II is showing comparison of efficacy parameters.

A total of 4 deaths (2 in each group) were reported. Abdominal distension was the commonest complication reported among 143 (51.1%) neonates while 129 (46.1%) and pulmonary hemorrhage 87 (31.1%) were some of the other most frequently observed complication. No major difference in terms of complications between both study groups was reported as shown in Table III (p>0.05)

Table 1: Characteristics of Study Participants (n=280)

Characteristics		Group-A (n=140)	Group-B (n=140)	P-Value
Gender	Male	66 (47.1%)	60 (42.9%)	0.471
	Female	74 (52.9%)	80 (57.1%)	
Gestational Age (weeks)	28 to 30	68 (48.6%)	75 (53.7%)	0.402
	31 to 34	72 (51.4%)	65 (46.3%)	
Weight (kg)	1-1.4	74 (52.9%)	70 (50.0%)	0.741
	1.5-1.9	42 (30.0%)	48 (34.3%)	
	2.0-2.4	24 (17.1%)	22 (15.7%)	
Length (cm)	≤43	86 (61.4%)	79 (56.4%)	0.675
	44-47	36 (25.7%)	42 (30.0%)	
	>47	18 (12.9%)	19 (13.6%)	
Antenatal administration of dexamethasone to mothers for RDS prevention		18 (12.9%)	16 (11.4%)	0.714

Discussion

We were unable to note any significant differences in terms of treatment failure (47.6% vs. 52.4%, p=0.4733) in the present study. Non-invasive respiratory support like NCPAP and HHHFNC are taken as best methods for providing assistance to preterm newborns having breathing issues.[11] In the recent years, HHHFNC has emerged as a popular option all around the world. Data from developing countries has found utilization of HHHFNC to be significantly increasing in 2015 as 87% in comparison to 56% during 2012.[12] However, developing countries lack data and outcomes related to HHHFNC among neonates with RDS. Majority of the trials have analyzed HHHFNC in preventing extubation failure among neonates with RDS while studies evaluating respiratory support of HHHNFC among preterm neonates is not very frequently seen.[13,14] Lavizzari A and colleagues analyzing HHHFNC versus NCPAP among premature neonates with RDS concluded comparative efficacy of HHHFNC when compared to NCPAP as primary approach.[15] The findings of the present study are consistent with the results of Lavizzari A et al as HHHFNC turned out to be an efficacious approach with similar complications profile when compared to NCPAP as primary mode of treatment.

Table II: Comparison of Efficacy Parameters among Both Study Groups

Efficacy	NCAP Group	HHHFNC Group	P-Value
Treatment Failure, n (%)	67 (47.6%)	73 (52.4%)	0.473
Surfactant Used, n (%)	71 (50.7%)	66 (47.1%)	0.550
Total duration of non-invasive ventilator (NIV) support required (hours), Mean±SD	219.1±68.7	228.8±74.9	0.259
Total duration (hours) of supplementary oxygen (hours), Mean±SD	28.4±4.3	29.1±4.7	0.194

Table III: Comparison of Complications among Both Study Groups

Complications	NCAP Group	HHHFNC Group	P-Value
Pneumothorax	14 (10.0%)	10 (7.1%)	0.393
Pulmonary Intersittial Empysema	3 (2.1%)	0 (0%)	0.542
Pulmonary Hemorrhage	42 (30.0%)	45 (32.1%)	0.698
Pneumonia	63 (45.0%)	67 (47.6%)	0.631
Decreased Cardiac Output	28 (20.0%)	34 (24.3%)	0.387
Abdominal Distension	76 (54.3%)	67 (47.6%)	0.2819
Intraventricular Hemorrhage	25 (17.9%)	34 (24.3%)	0.187
Death	2 (1.4%)	2 (1.4%)	1.000

Roberts CT et al found HHHFNC showed significantly increased rates of treatment failure in comparison to NCPAP when adopted as primary approach among preterm neonates with RDS.[16] Difference in findings between ours and Roberts CT et al studies could be due to the fact that they included 51.2% of neonates with gestational age below 32 weeks while we had all the study participants with gestational ages between 28 to 34 weeks. There could be a possibility that HHHFNC is better tolerated among more mature preterm neonates. Higher rates of treatment failure in the present stud could be due to the reasons that only 12.1% of the mothers in the present study had prenatal steroids.

Some researchers have analyzed role of HHHFNC as major approach in terms of respiratory support in the delivery room.[17] HHHFNC are small, thin, tapered bi-nasal tubes delivering oxygen or blended oxygen/air at gas flows of > 1 L/min.[18] HHHFNC is considered to be simple approach whereas inability of the certainty about the delivered airway distending pressure is one of the major drawbacks of this approach. Another important concern with HHHFNC is the probability of high, unmeasured recorded pressure up to 20 to 30 cm H_20 adopting flow rate above 2L/min.[19] We were unable to measure generated pressure in the present study. Chances of infection using HHHFNC are also reported by some researchers in the past.[20] One advantage with HHHFNC is small, lighter and usually short utilization, non-occulusive bi-nasal prongs that need heated water humidifier preventing nasal trauma. Abdominal distension was the most common complication recorded in the present study and it is a major factor that can be the reason of non-invasive ventilation failure requiring re-intubation.[21] There were some limitations of the present study. We were unable to detect pressure of HHHFNC in terms of flow parameters. We also could not differentiate whether thickness of the nasal catheter affects the clinical outcome or not.

Conclusion

HHHFNC had similar efficacy when compared to NCPAP among neonates with RDS. In comparison to NCPAP, HHHFNC could be a simple, well-tolerated and effective alternative in terms of respiratory support. No major difference in terms of complication was observed between both treatment approaches.

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