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Early high-flow nasal cannula versus continuous positive airway pressure as primary respiratory support in preterm neonates with respiratory distress: A prospective comparative cohort study

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Abstract

Background: Respiratory distress syndrome (RDS) remains a leading cause of morbidity in preterm neonates. Continuous positive airway pressure (CPAP) is the standard non-invasive respiratory support, but high-flow nasal cannula (HFNC) has emerged as a potential alternative due to ease of use and improved comfort. Evidence directly comparing HFNC and CPAP as primary respiratory support in preterm neonates remains limited. ***Objective***: To compare the efficacy, safety, and clinical outcomes of early HFNC versus CPAP as primary respiratory support in preterm neonates with respiratory distress. ***Methods***: This prospective comparative cohort study was conducted in a tertiary neonatal intensive care unit (NICU) over 18 months. A total of 100 preterm neonates (gestational age 28–34 weeks) with respiratory distress requiring non-invasive respiratory support within the first 6 hours of life were enrolled. Neonates received either HFNC or CPAP as primary support according to unit allocation protocol. Primary outcome was treatment failure requiring escalation to mechanical ventilation within 72 hours. Secondary outcomes included duration of respiratory support, oxygen requirement, nasal trauma, air leak syndromes, bronchopulmonary dysplasia (BPD), and mortality. ***Results***: Treatment failure occurred in 18% of the HFNC group and 14% of the CPAP group (p = 0.57). Mean duration of respiratory support was comparable between groups (HFNC: 4.6 ± 1.8 days vs CPAP: 4.9 ± 2.1 days; p = 0.42). Nasal trauma was significantly lower in the HFNC group (6% vs 22%, p = 0.02). No significant differences were observed in incidence of BPD, air leak, or mortality. ***Conclusion***: Early HFNC appears comparable to CPAP as primary respiratory support in preterm neonates with respiratory distress, with the added benefit of reduced nasal trauma. HFNC may be considered a safe and effective alternative to CPAP in selected preterm neonates.

Keywords: High-flow nasal cannula, CPAP, preterm neonates, respiratory distress syndrome, non-invasive ventilation.

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INTRODUCTION

Respiratory distress syndrome (RDS) is one of the most common causes of respiratory failure in preterm neonates and contributes significantly to neonatal morbidity and mortality worldwide[1]. The condition primarily results from surfactant deficiency and structural immaturity of the lungs, leading to atelectasis, impaired gas exchange, and increased work of breathing. Advances in neonatal care, including antenatal corticosteroids, early surfactant therapy, and non-invasive ventilation strategies, have substantially improved survival outcomes in preterm infants[2].

Continuous positive airway pressure (CPAP) has become the cornerstone of non-invasive respiratory support for preterm neonates with respiratory distress[3]. CPAP helps maintain functional residual capacity, reduces alveolar collapse, and improves oxygenation, thereby decreasing the need for mechanical ventilation and its associated complications. Despite its benefits, CPAP use is associated with challenges such as nasal trauma, poor tolerance, air leak syndromes, and the need for skilled nursing care[4].

High-flow nasal cannula (HFNC) therapy delivers heated, humidified gas at high flow rates through nasal prongs, generating a variable level of positive airway pressure. HFNC has gained popularity in neonatal practice due to its simplicity, improved comfort, ease of application, and reduced nasal injury. However, the pressure generated by HFNC is less predictable compared to CPAP, raising concerns about its effectiveness as a primary mode of respiratory support in preterm infants[5].

Several studies have evaluated HFNC as a step-down therapy following CPAP or mechanical ventilation, but evidence regarding its use as initial respiratory support remains inconclusive. The present study was designed to compare early HFNC and CPAP as primary respiratory support modalities in preterm neonates with respiratory distress, focusing on treatment failure, clinical outcomes, and complications[6].

MATERIALS AND METHODS

Study Design and Setting

This prospective comparative cohort study was conducted in the Neonatal Intensive Care Unit (NICU) of Shridevi Institute of Medical Sciences and Research Hospital, Tumakuru over a period of 18 months.

Ethical Approval

The study protocol was approved by the Institutional Ethics Committee. Written informed consent was obtained from parents or legal guardians prior to enrollment.

Study Population

Preterm neonates admitted to the NICU with signs of respiratory distress within the first 6 hours of life were screened for eligibility.

Inclusion Criteria:

- Gestational age between 28 and 34 completed weeks
- Onset of respiratory distress within 6 hours of birth (tachypnea, retractions, grunting, nasal flaring)
- Requirement for initiation of non-invasive respiratory support within 6 hours of birth

Exclusion Criteria:

- Major congenital anomalies
- Congenital heart disease (except PDA, ASD)
- Severe birth asphyxia (Apgar <3 at 5 minutes)
- Immediate need for mechanical ventilation

Sample Size

A total of 100 neonates were enrolled, with 50 neonates in each group (HFNC and CPAP), based on convenience sampling during the study period.

Allocation to Study Groups

Eligible neonates were allocated to receive either HFNC or CPAP as primary respiratory support according to the unit's predefined allocation protocol/availability of equipment (non-randomized allocation). Baseline demographic and clinical characteristics were recorded at admission.

Intervention

HFNC Group: Heated, humidified high-flow oxygen was delivered using nasal cannula at an initial flow rate of 4–6 L/min, titrated up to 8 L/min based on clinical response. Fraction of inspired oxygen (FiO_2) was adjusted to maintain target oxygen saturation between 90–95%.

CPAP Group: Bubble CPAP was delivered through appropriately sized nasal mask or nasal prongs at an initial pressure of 5 cm H_2O, titrated up to 7 cm H_2O as required. FiO_2 was adjusted to maintain oxygen saturation between 90–95%.

Monitoring

Neonates were continuously monitored for heart rate, respiratory rate, oxygen saturation, work of breathing, and apnea. Arterial or capillary blood gases were obtained when clinically indicated.

Outcome Measures

Primary Outcome

Treatment failure, defined as the need for intubation and mechanical ventilation within 72 hours of initiation of non-invasive support due to any of the following:

- $FiO_2 > 0.60$ to maintain $SpO_2 \geq 90\%$
- Recurrent apnea (>3 episodes/hour or requiring stimulation)
- Respiratory acidosis (pH < 7.25 with $PaCO_2 > 60$ mmHg)
- Persistent or worsening respiratory distress

Secondary Outcomes

- Duration of respiratory support (days)
- Duration of oxygen therapy (days)
- Incidence of nasal trauma (erythema, ulceration, or bleeding requiring intervention)
- Air leak syndromes (pneumothorax/pulmonary interstitial emphysema)

- Bronchopulmonary dysplasia (oxygen requirement at 36 weeks postmenstrual age)
- Mortality before discharge

Data Collection:
Demographic data, perinatal variables, clinical parameters, and outcomes were recorded prospectively using a structured data collection form.

Statistical Analysis
Data were analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation and compared using Student's *t*-test. Categorical variables were compared using Chi-square or Fisher's exact test. A *p*-value <0.05 was considered statistically significant.

RESULTS

Both groups were comparable in terms of gestational age, birth weight, sex distribution, and severity of respiratory distress at admission.

Table 1: Baseline Characteristics of Study Population

Variable	HFNC (n=50)	CPAP (n=50)	p-value
Gestational age (weeks), mean±sd	32.4 ± 2.1	32.1 ± 2.3	0.48
Birth weight (g), mean±sd	1650 ± 320	1605 ± 340	0.52
Male sex, n(%)	28 (56)	30 (60)	0.68
Antenatal steroids, n(%)	39 (78)	41 (82)	0.61

Treatment failure rates were similar between the two groups.

Table 2: Primary Outcome

Outcome	HFNC (n=50)	CPAP (n=50)	p-value
Treatment failure,n (%)	9 (18)	7 (14)	0.57

Table 3: Respiratory and Clinical Outcomes

Outcome	HFNC	CPAP	p-value
Duration of respiratory support (days), mean±sd	4.6 ± 1.8	4.9 ± 2.1	0.42
Duration of oxygen therapy (days), mean±sd	6.2 ± 2.4	6.5 ± 2.6	0.58
Bronchopulmonary dysplasia, n (%)	5(10)	6(12)	0.75

Table 4: Complications and Mortality

Complication	HFNC	CPAP	p-value
Nasal trauma, n(%)	3 (6)	11 (22)	0.02
Air leak syndrome	2 (4)	3 (6)	0.64
Mortality	2 (4)	2 (6)	0.64

DISCUSSION

In this prospective comparative cohort study, early use of HFNC as primary respiratory support demonstrated clinical outcomes comparable to those of CPAP in preterm neonates with respiratory distress. The rate of treatment failure requiring mechanical ventilation did not differ significantly between groups, suggesting that HFNC may provide adequate respiratory support in appropriately selected preterm infants [7].

A notable finding of the present study was the significantly lower incidence of nasal trauma in the HFNC group. Nasal injury is a well-recognized complication of CPAP therapy and may lead to discomfort, feeding difficulties, interruption of respiratory support, and prolonged hospital stay [8–9]. The reduced nasal trauma observed with HFNC is consistent with previous reports and likely reflects the softer interface and lower local pressure exerted on the nasal tissues. Improved tolerance and ease of handling may also enhance caregiver compliance and overall patient comfort.

The duration of respiratory support and oxygen therapy was similar in both groups, indicating comparable efficacy in maintaining respiratory stability and oxygenation. Furthermore, no significant differences were observed in important neonatal outcomes such as air leak syndromes, bronchopulmonary dysplasia, or mortality. These findings align with earlier studies that have reported non-inferiority of HFNC compared with CPAP in selected preterm populations [10–12].

Despite these encouraging results, certain considerations are important. The airway pressure generated by HFNC is variable and influenced by factors such as flow rate, cannula size, and mouth leak. Consequently, extremely preterm or more

severely ill neonates may require closer monitoring and timely escalation of support. Clearly defined criteria for treatment failure and vigilant clinical assessment remain essential when HFNC is used as primary therapy.

The strengths of this study include its prospective design and systematic evaluation of clinically relevant outcomes. However, several limitations must be acknowledged. The study was conducted at a single center with a relatively small sample size, which may limit generalizability. In addition, the non-randomized allocation could introduce selection bias. Therefore, larger multicenter randomized controlled trials are needed to further validate these findings and establish standardized protocols for HFNC use in preterm neonates.

Overall, our findings suggest that HFNC appears to be a safe and effective alternative to CPAP as initial non-invasive respiratory support in preterm neonates, with the added advantage of reduced nasal trauma and improved tolerance.

CONCLUSION

Early use of high-flow nasal cannula appears to be a safe and effective alternative to CPAP as primary respiratory support in preterm neonates with respiratory distress. HFNC offers comparable efficacy with the advantage of reduced nasal trauma and improved tolerance. Larger randomized controlled trials are recommended to further validate these findings.

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