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REVIEW ARTICLE

# Effectiveness of High-flow Nasal Cannula (HFNC) over Continuous Positive Airway Pressure (CPAP) as A Primary Mode of Respiratory Support in Children : A Review

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**Abstract**

*HFNC provides heated, humidified gas which minimizes metabolic cost and eliminate effects of cooling and drying. It optimizes oxygenation, meets inspiratory demand and decreases inspiratory and expiratory work of breathing also wash out of pharyngeal dead space and helps in $CO_2$ removal. It's use has been expanded to all causes of acute hypoxemic respiratory failure, especially in bronchiolitis, and in post-extubation respiratory failure as well, starting from Emergency Department, Pediatric Ward, Pediatric Intensive Care Unit (PICU), Neonatal Intensive Care Unit (NICU) and during transportation. It is well tolerated than CPAP, BiPAP and NIPPV. Continuous positive airway pressure (CPAP) is frequently used as the recommended treatment option for respiratory distress but it has some adverse events. In this review it is not about comparing HFNC with CPAP, because both comparisons are not of equal modalities, it is to understand what is the right place of HFNC therapy in children.*

***Keywords*: *High-flow nasal cannula (HFNC), continuous positive airway pressure (CPAP), respiratory support, children.***

## Introduction

Respiratory distress is one of the most common presenting problems in pediatric patients and requires immediate attention. Primary respiratory support by using non-invasive methods are becoming popular day by day. Although Continuous positive airway pressure (CPAP) is frequently used as the recommended treatment option there are problems with the use of CPAP like difficulties in maintaining the nasal prongs in the nostrils, granulation, ulceration, necrosis, nasal vestibular stenosis, nasal deformities, poor tolerance of the infant to the apparatus, difficulties in positioning the neonate and increased nursing time and a need for skilled nursing staff.[1-3]

Heated humidified high-flow nasal cannula (HHHFNC) is a newly emerged non-invasive respiratory support that has been increasingly applied and recently gained popularity. A number of studies suggest that it is superior to CPAP because it protects airway mucosa, increases gas exchange and lowers respiratory work.[4,5]

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HFNC is widely used in conditions like bronchiolitis, pneumonia and acute hypoxemic respiratory failure. Studies have shown that HFNC can significantly improve oxygenation and reduce the need for intubation in children with moderate to severe respiratory distress. It is particularly effective in managing viral bronchiolitis, where it helps in reducing hospital stay and intensive care admissions.[6]

Despite its widespread use, there is still lack of standardized guidelines for HFNC application in pediatric care. The heterogeneity in study designs and settings makes it challenging to establish universally accepted protocols. More randomized controlled trials are needed to further delineate the optimal flow rates and clinical indications for HFNC in various pediatric respiratory conditions.[6]

**Rationale of using heated humidified high-flow nasal cannula**

The rationale behind HFNC therapy is to provide high flows, at a higher rate than the patient's peak inspiratory flow rate (PIFR), in order to overcome the high needs of a patient in respiratory distress.[7] Historically, Standard Oxygen Therapy (SOT) is provided on low flow ≤2 L/min oxygen, without or with very little cold bubble humidification in the Emergency Department and in Pediatric Wards, which is not capable of delivering the optimum hydration level at the most favorable function of the respiratory system. The exact amount of oxygen administration is rarely known and approximations are made depending on the oxygen flow and the air mixing from the environment, according to the peak inspiratory flow generated by the patient's respiratory effort. $O_2$ is a dry gas and if we use $O_2$ long time it can cause dryness and irritation of respiratory mucous membrane which interfere respiratory ciliary function. When the gas is not properly humidified it increases energy expenditure and metabolic demand. Low flow increases inspiratory resistance in nasopharynx and alveoli. A system that could deliver a warm, well-hydrated, precise oxygen level, would have been ideal. By using HFNC heated humidified gas by eliminating the drying & cooling effects of airway: improves lung and airway mechanics and reduce metabolic demand of the body. Though HFNC is generally well-tolerated, there is a need for careful monitoring to avoid complications such as air leak syndrome. Guidelines suggest starting with a flow rate of 1-2 L/kg/min, with a maximum of 10-12 L/min for infants and up to 50 L/min for older children and adults.[8]

**Effectiveness of HFNC over CPAP as a primary mode of respiratory support**

Liu et al[9] conducted a prospective randomized controlled study, where 84 patients with pneumonia having mild to moderate respiratory failure admitted to the Children's Hospital Affiliated to Chongqing Medical University from January 2018 to December 2019 were randomly divided into the HFNC group and the CPAP group. Treatment failure necessitating intubation and transfer to the PICU was noted in 6(14%) of 43 infants in the HFNC group, as compared with 4(10%) of 41 infants in the CPAP group ($p>0.05$). There were no significant differences between the two groups in the duration of hospital stay, the duration of non-invasive respiratory support and mortality. HFNC resulted in lower rate of air leaks, nasal trauma, abdominal distension and later time of mechanical ventilation initiating, less duration of oxygen therapy and earlier enteral feeding.

In Bangladesh Chisti et al[10] conducted an open RCT where 225 eligible children were recruited with severe pneumonia and hypoxemia showed that, there was no difference in treatment failure between patients in the CPAP group and the HFNC group.

A systemic review by Zayed et al[11] included 16 studies involving 2,180 subjects found that, non-invasive ventilation (NIV) was associated with a significant reduction in intubation rates compared with conventional oxygen therapy, but there was no significant difference in the efficacy with HFNC. But the results were different from those of the meta-analysis of 8 studies included 2259 subjects below 5 years of age on HFNC vs. CPAP in children with respiratory distress by Luo et al.[12] They found that, CPAP may be superior to HFNC in the treatment of moderate to severe respiratory distress and severe hypoxemia in infants aged 1-6 months, but no significant difference was observed between the two groups in infants aged 6-12 months.

In a randomized controlled trial, Vahlkvist et al[13] examined the improvement of respiratory rate, $PCO_2$ and Modified Wood's Clinical Asthma Score (MWCAS) in over fifty children with bronchiolitis and discovered no differences. NIPS (Neonatal Infant Pain Score) was higher in the CPAP group. Treatment

failure was scarce in both groups. No significant differences in treatment duration or length of hospitalization were observed.

Milési et al[14] conducted a randomized controlled trial where 142 infants were allocated to the 2-L/kg/min (2L) flow rate and 144 infants to the 3-L/kg/min (3L) flow rate. Failure rate was comparable between groups: 38.7% (2L) vs. 38.9% (3L; p=0.98). Worsening respiratory distress was the most common cause of failure in both groups: 49% (2L) vs. 39% (3L; p=0.45). In the 3L group, discomfort was more frequent (43% vs. 16%, p=0.002) and PICU stays were longer (6.4 vs. 5.3 days, *p*=0.048). The intubation rates [2.8% (2L) vs. 6.9% (3L), p=0.17] and durations of invasive [0.2 (2L) vs. 0.5 (3L) days, p=0.10] and noninvasive [1.4 (2L) vs. 1.6 (3L) days, p=0.97] ventilation were comparable. They concluded that, young infants with acute bronchiolitis supported with HFNC, 3 L/kg/min did not reduce the risk of failure compared with 2 L/kg/min.

An observational cohort study was conducted by Hegde et al[15] in a tertiary care level III neonatal intensive care unit included 88 preterm infants between 28 to 34 weeks of gestation with mild to moderate respiratory distress within 6 hours of birth. They found that, there was no difference in the requirement of mechanical ventilation between HFNC (19.5%) and CPAP (26.2%) groups (p=0.46). Moderate or severe nasal trauma occurred less frequently with HFNC (10.9%) in comparison to CPAP (40.5%) (p= 0.004).

Yoder et al[16] conducted a randomized controlled unblinded non crossover trial, that included 432 infants ranging from 28 to 42 weeks' gestational age. They found that, there was no difference in early failure for HFNC (23/212 [10.8%]) versus CPAP (18/220 [8.2%]; p=0.344), subsequent need for any intubation (32/212 [15.1%] vs 25/220 [11.4%]; p=0.252) or in any of several adverse outcomes, including air leak. HFNC infants remained on the study mode significantly longer than CPAP infants (median: 4 vs 2 days, respectively; p<0.01), but there were no differences between study groups for days on supplemental oxygen (median: 10 vs 8 days), bronchopulmonary dysplasia (20% vs 16%) or discharge from the hospital on oxygen (19% vs 18%).

In 2020 a study was conducted by Charki et al[17] in a neonatal intensive care unit in North Karnataka, India. In this study, all preterm neonates less than 37 weeks of gestation were placed on one of the respiratory supports (HFNC or CPAP), immediately following extubation from mechanical ventilation. There were no significant differences in major clinical outcomes including death, BPD, ventilator days, necrotizing enterocolitis, severe intraventricular hemorrhage, retinopathy of prematurity or time to full feeds. Failure of assigned mode of respiratory support was seen in 12% of infants on HFNC compared to 16% on CPAP (p = 0.48). No significant difference in other outcome measures was seen between the groups. No nasal injury was observed in the HFNC group against 10% in the CPAP group (p=0.55).

Manley et al[18] conducted a multicenter, randomized, noninferiority trial and assigned 303 very preterm infants to receive treatment with either HFNC (5 to 6 liters per minute) or nasal CPAP (7 cm of water) after extubation. They found that, the use of HFNC was noninferior to the use of CPAP, with treatment failure occurring in 52 of 152 infants (34.2%) in the HFNC group and in 39 of 151 infants (25.8%) in the CPAP group (risk difference, 8.4 percentage points; 95% confidence interval, -1.9 to 18.7). Almost half the infants in whom treatment with HFNC failed were successfully treated with CPAP without reintubation. The incidence of nasal trauma was significantly lower in the HFNC group than in the CPAP group (p =0.01), but there were no significant differences in rates of serious adverse events or other complications.

A meta-analysis by Wilkinson et al[19] observed six studies, including 934 neonates who were randomized to either HFNC or CPAP as post extubation means of respiratory support. They demonstrated that, no additional risk of treatment failure in the HFNC group. It also suggested that in neonates from 28 to 32 weeks of gestation, HFNC (with the availability of rescue CPAP) may be an appropriate modality of respiratory support.

Iskandar et al[20] conducted a randomized, non-inferiority, clinical trial using HFNC vs. CPAP as a treatment for moderate respiratory distress within 72 hours after birth over 169 babies. They observed that, no differences were in terms of incidence of endotracheal intubation within <72 hours of HFNC (20%) compared to CPAP (18%) (p =0.799). However, there was a significant difference in moderate nasal trauma in CPAP (14%) compared to HHHFNC (0%)

(p=0.006). There were no significant differences of blood gas analysis results, full enteral feeding time, length of KMC, length of device uses and rate of complications (bronchopulmonary dysplasia/BPD, intraventricular hemorrhage/ IVH, patent ductus arteriosus/PDA, necrotizing enterocolitis/NEC and late onset neonatal sepsis/LONS) between the CPAP and HFNC groups.

**Conclusion**

HFNC is a valuable tool in pediatric respiratory care, offering several benefits over traditional methods. HFNC appears to have similar efficacy and safety to CPAP when applied as a primary mode of respiratory support in infant and children even in preterm infants with respiratory distress as well as post extubation means of respiratory support with low complication rate. However, careful patient selection and monitoring are essential to maximize its efficacy and safety. Continued research and development of standardized guidelines will help optimize its use in clinical practice.

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