

Review Article

The role of high-flow nasal cannula in pediatric respiratory distress

Abdullah Y. Alnewirah^{1*}, Abdulaziz H. Alluhaibi¹, Abdullah F. Altowairqi²,
Sara M. Alosaimi², Alhasan M. Aljohani²

¹Department of Pediatrics Emergency Medicine, Maternity and Children's Hospital, Makkah, Saudi Arabia

²Department of Pediatrics, Taif Children Hospital, Taif, Saudi Arabia

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*Correspondence:

Dr. Abdullah Y. Alnewirah,

E-mail: abdullah.alnewirah@gmail.com

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ABSTRACT

Recently, high-flow nasal cannula (HFNC) oxygen therapy has been introduced as a non-invasive ventilation therapy in pediatric populations. It has shown great efficacy in managing respiratory distress in adult populations, and it has been associated with promising outcomes in pediatrics through the last two decades. HFNC provides heated and humidified air mixed with oxygen through a nasal cannula, resulting in better oxygenation and reduced respiratory distress. Additionally, it has a basic principle, which is setting oxygen flow higher than inspiratory demand flow based on the clinical situation. HFNC was originally used in pediatric intensive care units; however, its use has expanded to various pediatric settings and different respiratory conditions, such as bronchiolitis and asthma. Although evidence exploring the effectiveness of HFNC in managing respiratory distress in pediatrics has steadily grown, it is still limited compared to evidence on adults. This review explores the effectiveness of HFNC in pediatric respiratory distress, highlighting its implications and adverse effects. Current evidence shows that HFNC efficacy is comparable to other non-invasive ventilation modalities or higher in some cases. It is also considered generally safe, as it is associated with fewer adverse events and is easier to use. These results encourage further research focusing on the use of HFNC in more uncommon and severe respiratory distress conditions in pediatrics.

Keywords: High-flow nasal cannula, HFNC, Pediatric, Respiratory distress, Non-invasive ventilation

INTRODUCTION

High-flow nasal cannula (HFNC) oxygen therapy was first used in clinical practice as another option for continuous positive airway pressure (CPAP), in the early 2000s, to treat apnea in premature infants.¹ Thereafter, the use of HFNC in pediatric populations has steadily grown. Currently, HFNC is a greatly preferred mode of respiratory support in pediatric care due to the availability of easy-to-use devices, which can be remarkably well tolerated by adult and pediatric patients when compared to CPAP or other modes of non-invasive ventilation (NIV).² HFNC apparatus act through providing heated and humidified air mixed with oxygen at various flow rates and adjustable concentrations. A comfortable and soft silicone nasal cannula is used to inhale the gas, and this cannula fits without occluding the nose.³

The term "high flow" is typically contrasted with "low flow" in conventional oxygen therapy (COT); however, there is no exact definition of what qualifies as high flow in HFNC. The flow rates vary based on the patient's age and weight, ranging from 2 to 60 l/min.^{4,5} Although HFNC was typically limited to pediatric intensive care units (PICU), it has extended to various settings, such as inpatient pediatric wards, emergency departments, and even patients' homes due to its efficacy and ease of use.^{5,6} Although evidence exploring the effectiveness of HFNC in managing respiratory distress in pediatrics has steadily grown, it is still limited compared to evidence on adults.³

Furthermore, the application of HFNC in various uncommon pediatric respiratory conditions, such as obstructive sleep apnea (OSA), is still not fully established.

Thus, the aim of this review is to summarize current evidence discussing the role of high-flow nasal cannula in pediatric respiratory distress. This review focuses on the mechanisms of action of HFNC, its clinical implications, and the potential future perspectives.

HFNC SYSTEM

HFNC is presently offered in three variants for pediatric patients.³ The first type, utilized by Comfort-Flo® (Teleflex Medical, Durham, NC, USA), Precision Flow® (Vapotherm, Exeter, UK), and the Optiflow® System (Fisher & Paykel, Auckland, New Zealand), consists of an oxygen/air blender connected to a heating and humidification system (Figure 1). This device can incorporate a pressure relief valve that halts airflow once the circuit reaches a specified pressure threshold.

The second type, exemplified by the Airvo2® (Fisher & Paykel, Auckland, New Zealand), incorporates an integrated turbine-driven flow generator with a heated humidifier. Unlike the first type, this system does not

require an external gas source, except for nitric oxide and oxygen, when clinically indicated.

The third type operates via a conventional ventilator or CPAP system, utilizing an HFNC breathing circuit connected to a humidifier to deliver high-flow therapy.³

Currently, there is no universal agreement between pediatricians about the optimal flow. Therefore, data about convenient flow was extracted from the most relevant clinical studies in acute bronchiolitis in pediatrics.⁷⁻⁹ It was observed that children <24 months could tolerate a flow of 1–2 l/kg/min (up to 20 l/min). While higher flows showed the same reported efficacy but reported as uncomfortable.⁹ Flow recommendations according to child weight are as follows: 1–2 l/kg/min are recommended up to 10 kg; 1 l/kg/min for 10–20 kg; 0.8–1 l/kg/min for 20–40 kg; 0.5–1.1 l/kg/min for >40 kg.^{3,9} Cannula size also has to be chosen according to body weight and age. The cannula's cross-sectional area should be no more than 50% of the nostrils to prevent unexpected rises in airway pressure and the associated risk of air leakage.³

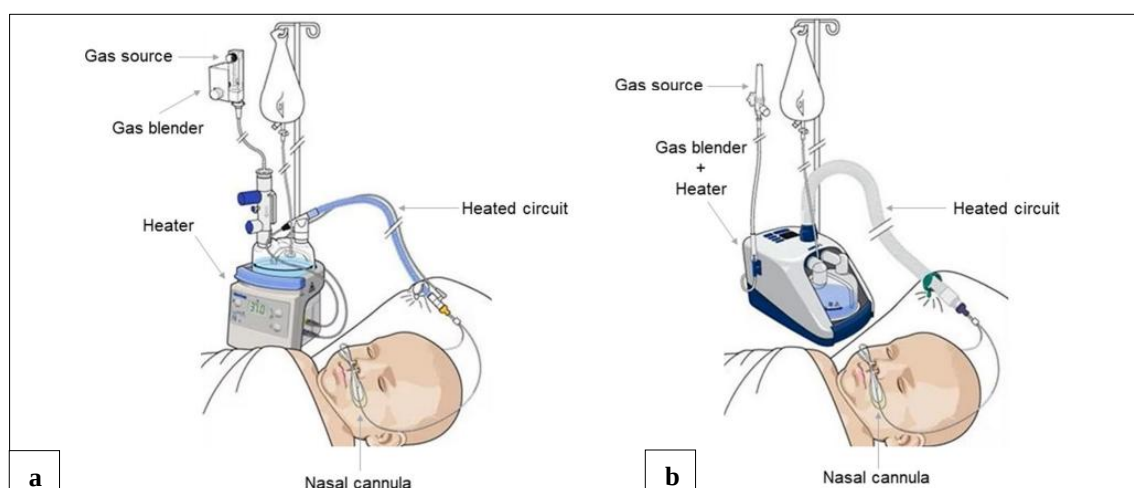


Figure 1: (a) Fisher and Paykel optiflow system, and (b) Fisher and Paykel Airvo 2 ® system. Both allow an inhaled oxygen fraction of up to 100% and generate a flow of up to 60 l/min. The Fisher and Paykel Airvo 2 ® system combines a gas mixer and heater in one device.

Using HFNC for drug delivery is a desirable modality of administration as traditional nebulizer masks are usually poorly tolerated by children.¹⁰ Despite this advantage, conflicts emerged after evaluation of some *in vitro* feasibility. The HFNC shows two major limitations: the aerosol administration through nasal cannulas elevates the upper airways deposition compared to oral inhalation; and high flow rate of gas elevates particle deposition by impaction.^{11,12} These studies stated that aerosol particle distribution is only possible at flows <6 l/min.¹⁰

MECHANISM OF ACTION AND PHYSIOLOGICAL EFFECTS OF HFNC

High flow nasal cannulas exert their action through adjusted (FiO_2 21–100%) and heated (34–37°C) oxygen

with nearly 100% relative humidity.¹³ This can protect against mucosal injury and patient discomfort from cold and dry air. Furthermore, heated humidification can induce secretion clearance and decrease bronchoconstriction.¹³ HFNC has a basic principle, which is setting oxygen flow higher than inspiratory demand flow based on the clinical situation, resulting in reduced dead space, decreased nasal resistance, and washout of the upper airways.¹⁴ In addition, recent studies demonstrated that HFNC stimulates positive airway pressure, leading to the elevation of functional residual capacity and alveolar recruitment of collapsed lesions.^{15,16} HFNC also enhances oxygenation, minimizes the dilution of wanted gas composition, and reduces the inflow of ambient air.¹⁷ Notably, no age-dependent differences between adults and children in its mechanism of action were observed.

CLINICAL IMPLICATIONS OF HFNC

Bronchiolitis

Acute bronchiolitis is one of the most prevalent diseases in the pediatric population, especially those under 2 years.¹⁸ It can be caused by various microorganisms; however, respiratory syncytial virus is considered the most common causative organism.¹⁸ Recently, it has been observed that the current standard of care with COT is being replaced by HFNC, particularly in patients with moderate-to-severe acute bronchiolitis.³ Recent large clinical trials evaluated the effectiveness of HFNC in managing acute bronchiolitis compared to COT and found a lower rate of treatment failure in the HFNC group.^{7,8} However, HFNC and COT demonstrated similar effects on PICU admission, duration of oxygen therapy, and duration of hospital stay. Another recent systematic review compared the effectiveness of COT, CPAP, and HFNC in acute bronchiolitis.¹⁹ The study reported a superiority for CPAP and HFNC over COT; however, HFNC group showed significantly more frequent treatment failure events when compared to the CPAP group. These negative results of HFNC could be attributed to an important limitation, addressed by Catano-Jaramillo and colleagues in their meta-analysis, which is the inclusion of patients with any degree of bronchiolitis severity, without performing a subgroup analysis in children with moderate-to-severe bronchiolitis.²⁰ They also demonstrated that both HFNC and CPAP decreased intubation risk; however, CPAP was associated with a lower rate of therapeutic failures, asserting the previous results also in this cluster of patients. Notably, although CPAP showed superiority over HFNC, it was less tolerated and resulted in more adverse events, including skin lesions.²⁰ Available data indicate that while HFNC is superior to COT, it remains inferior to CPAP. However, due to its ease of use and safety, it can still be used as an emergency treatment for patients with moderate-to-severe bronchiolitis.³

Asthma

High-flow nasal cannula oxygen therapy can support the respiratory system during asthma exacerbations by reducing the work of breathing. Additionally, the use of humidified and heated gas inhibits cold, dry gas-induced bronchoconstriction and enhances airway cilia movement, stimulating the mobilization of mucus plugs, a hallmark of acute asthma attacks.²¹ Two recent retrospective studies assessed the use of HFNC during asthma exacerbation and demonstrated that treatment with HFNC improved SpO₂/FiO₂ ratio, heart rate, respiratory rate, CO₂ tension, and pH level after 3–24 hours compared to COT.^{22,23}

A prospective pilot trial by Ballesterio et al confirmed these results.²⁴ HFNC and COT were examined in 62 children (1–14 years) with moderate to severe asthma exacerbations. After two hours of treatment, 53% of the children in the HFNC group showed a reduced pulmonary score by at least 2 points, while 28% of the COT group

showed a similar reduction ($p=0.01$).²⁴ However, no differences in hospital length of stay and PICUs admission were observed between the two groups. Another retrospective analysis compared the effectiveness of HFNC to NIV on managing asthma exacerbations.²⁵ In this study, 20 children received HFNC, 8 of them escalated to NIV, whereas 22 children received NIV without failure of treatment ($p<0.001$). This study stated that using HFNC over NIV should be done cautiously, as it may potentially delay the initiation of NIV, leading to longer periods of respiratory support and hospital stay.

Obstructive sleep apnea

Obstructive sleep apnea is characterized by upper airway obstruction during sleep.²⁶ OSA elevates risk for cardiovascular and neurocognitive conditions in children.^{27,28} Currently, OSA in children is treated by adenotonsillectomy, when applicable, and CPAP.²⁹ However, CPAP is usually restricted by limited adherence.³⁰ In 2009, 12 children with mild to severe OSA received high flows (20 l/min). This study by McGinley et al showed a decrease in the apnea-hypopnea index on HFNC that was comparable to that on CPAP.³¹ Two other recent observational studies examined the use of HFNC in CPAP-intolerant children with moderate-to-severe OSA and found improved oxygen saturation and reduced nocturnal respiratory events with HFNC.^{32,33} Furthermore, a case series demonstrated that long-term use of HFNC at home was successful in treating 5 children with severe OSA.³⁴ Despite the limited evidence, HFNC may be considered a rescue option for children who are uncooperative with CPAP treatment. Despite that, RCTs comparing HFNC and CPAP are required to establish definitive conclusions.

HFNC IMPLEMENTATION IN PEDIATRIC EMERGENCY DEPARTMENTS

The success of HFNC in treating respiratory distress in critically ill children and adults encouraged the use of HFNC in the pediatric emergency department (ED).⁴ Its ability to decrease the need for invasive mechanical ventilation (MV), better safety profile, and ease of use also foster HFNC initiation in the pediatric ED.³⁵ A recent study found that, after HFNC introduction, there was a reduction in overall intubation rates from 15.8% to 8.1% ($p=0.006$) and a decrease in pediatric intubations in ED from 10.5% to 2.2% ($p<0.001$).³⁵

As mentioned, multiple studies reported that HFNC is effective as other NIV modalities or even higher, in some cases, in managing various pediatric respiratory distress conditions in PICU and other settings. However, no prospective trials specifically address HFNC's effect on pediatric ED patients, so findings must be generalized with caution.⁴ HFNC is recommended for pediatric ED patients with moderate to severe respiratory distress as a primary support or after an unsuccessful standard nasal cannula trial.⁴

Multiple recent studies compared standard nasal cannula with HFNC. A recent observational study showed that the use of HFNC in pediatric ED patients with bronchiolitis led to shorter hospitalization and faster dyspnea enhancement compared to standard nasal cannula.³⁶ In addition, HFNC initiation in bronchiolitis patients in the ED was associated with a four-fold lower PICU transfer rate than standard NC-treated controls.⁵ However, several trials demonstrated mixed results in hospitalization length and oxygen therapy duration when comparing HFNC and standard NC, with cost-effectiveness playing a key role in decision-making.^{7,37} In summary, HFNC is a critical modality of respiratory support in pediatric emergency departments due to its safety, effectiveness, and fair cost-effectiveness.³⁵

HFNC IN PRETERM INFANTS

In preterm infants after birth, the most common morbidity is respiratory failure that requires noninvasive support with nasal modes of ventilation or invasive support with MV.³⁸ Survival rates of extreme preterm infants, as well as numbers requiring respiratory support, are rising according to multiple recent studies.^{38,39} HFNC is the most recent mode of ventilation to be used in preterm infants. Although evidence supporting its use is not fully established, it has rapidly been preferred by clinicians globally.^{6,40-44} Recently, multiple clinical trials have explored the use of HFNC in preterm infants both as a primary mode of support at birth and after extubation from MV. Furthermore, a recent meta-analysis study assessed the effectiveness of HFNC in treating respiratory distress in preterm infants and compared it with other NIV modes, such as noninvasive positive pressure ventilation and CPAP.⁴⁵

This study reported that other modes of NIV are not superior to HFNC in preterm infants. It also suggested that HFNC might be a preferred method in this gestational age, since it has significantly lower odds of nasal trauma and showed no remarkable differences in other common neonatal outcomes.⁴⁵ However, using HFNC in the extreme preterm group of infants should be cautious, since its efficacy and safety, either as a primary mode of support or after extubation, remain not fully established. Therefore, further research should focus on the extreme preterm group of infants, who could benefit most from modes of NIV. Weaning from NIV is another area of practice that requires further research, as a recent review on weaning HFNC in preterm infants found no eligible studies on the topic.⁴⁶

SAFETY AND ADVERSE EVENTS OF HFNC

If used within its clinical parameters, HFNC is considered generally safe. Adverse events of HFNC are mainly mild, including aerophagia, skin irritation caused by the cannula interface, and epistaxis.⁴ Serious complications are very rare; however, pulmonary air leak cases (pneumomediastinum or pneumothorax) have been reported in older children receiving HFNC.⁴⁷ Furthermore,

a case of pneumocephalus in a premature neonate has been reported.⁴⁸ These reports highlight the necessity of delivering HFNC through an “open system” with an appropriately sized non-occlusive cannula, which permits ample gas leak between the prongs and the surrounding nostrils. Additionally, this open system guarantees that the prongs of the nasal cannula are non-occlusive; therefore, decreasing the risk of sudden elevations in airway pressure because of inadvertent obstruction.⁴ Notably, pulmonary air leak incidence in vulnerable preterm patients was similar between patients treated with nasal CPAP or HFNC.⁴⁵ Moreover, in patients receiving HFNC, skin breakdown incidence was lower than in patients receiving a nasal CPAP interface, which needs pressure onto the skin surface to make an occlusive seal.⁴⁵

FUTURE DIRECTIONS AND RESEARCH GAPS OF THE HFNC

High-flow nasal cannula oxygen therapy can be promising in the management of other pediatric respiratory distress diseases such as bronchiectasis and cystic fibrosis.³ Both are characterized by chronic mucus secretion; thus, enhancing the mucociliary clearance is critical in these conditions to prevent recurrent infections, preserving long-term function.⁴⁹ HFNC can improve these conditions through the effects of humidified and heated gas flows on the airway cilia. Unfortunately, there are no published studies examining the effect of HFNC on pediatric patients with cystic fibrosis to date. On the other hand, only two case reports were published assessing the effectiveness of the use of long-term HFNC at home in children with bronchiectasis with a decrease in the incidence of pulmonary infection.^{50,51}

Interhospital transport is considered a critical moment for an ill child. 30% of whole PICU admission is attributed to clinical deterioration following interhospital transport. It also leads to an increased rate of invasive ventilation use and prolonged PICU stay.⁴⁹ In 2021, an Australian study showed that HFNC usage on interhospital transport was associated with decreased respiratory support use and PICU length of stay, thus supporting its employment in this setting.⁵² Furthermore, multiple case reports discussed the effects of HFNC in a pediatric burn patient with post-extubation stridor and in children with acute pulmonary edema.^{53,54}

CONCLUSION

High-flow nasal cannula oxygen therapy has been recently an effective mode of respiratory support in pediatric respiratory distress conditions, since it provides multiple benefits, including reduced respiratory distress, improved oxygenation, and enhanced patient comfort. Currently, HFNC is being used in different conditions, such as asthma, obstructive sleep apnea, bronchiolitis, and neonatal respiratory distress. It showed similar efficacy or, in some cases, higher than conventional oxygen therapy. Despite its advantages, limitations remain, particularly in

optimizing flow settings, drug delivery, and long-term outcomes. Further research, including randomized controlled trials, is needed to refine HFNC protocols and expand its potential applications in pediatric respiratory management.

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