HIGH-FLOW NASAL CANNULA (HFNC) THERAPY FOR NEONATES

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I. OVERVIEW

1.1. Concept

High-Flow Nasal Cannula (HFNC) therapy is a non-invasive respiratory support method that delivers a blend of air and oxygen at flow rates equal to or exceeding the patient's inspiratory demand. It helps reduce the work of breathing, provides positive end-expiratory pressure (PEEP), washes out dead space, and preserves the respiratory mucosa using heated and humidified gas. The gas flow rate provided to the patient can range from 2 to 60 L/min.

The first High-Flow (HFNC) delivery devices were introduced around the 2000s, and several studies on the application of HFNC showed a significant reduction in intubation rates among children in pediatric intensive care and neonatal emergency units.

Many scientific studies and clinical practice guidelines on HFNC from medical societies worldwide, such as the European Respiratory Society [1], the European Society of Intensive Care Medicine [2], and the American Association for Respiratory Care [3], have been published. Guidelines from these global societies agree on the efficacy, timing of use, and benefits of HFNC in reducing intubation rates or facilitating early weaning from mechanical ventilation in respiratory diseases, thereby reducing hospital length of stay and treatment costs.

A study using HFNC on 298 children under 24 months of age with bronchiolitis, upper airway obstruction, and cardiovascular/neuromuscular diseases showed a reduction in the intubation rate in the Intensive Care Unit from 37% to 7% [4].

Another study in the US on 848 children with a mean age of 4.6 years suffering from bronchiolitis showed a reduction in intubation rates from 11% to 2% [5].

Several randomized controlled trials (RCTs) have compared the efficacy of HFNC and CPAP following extubation in neonates.

	Manley *et al.* **2013**	**Collins** *et al.* **2013**	**Yoder** *et al.* **2013**
N	303 infants < 32 weeks Gestational Age (GA)	132 infants < 32 weeks GA	432 term and preterm infants > 28 weeks GA or > 1kg
Research design	Multicenter RCT	Single-center RCT	Multicenter RCT
Margin	20%	20%	20%
Flow (L/min)	5 - 8	4 - 8	3 - 8
CPAP (cm H_2O)	5 - 8	4 - 8	5 - 8
Outcome	Treatment failure within 7 days	Treatment failure within 7 days	Treatment failure within 72 hours

Conclusions from these studies suggest that HFNC can replace CPAP when the infant is clinically stable but still requires respiratory support greater than low-flow oxygen.

Studies comparing HFNC and CPAP in the initial management of respiratory distress immediately after birth show that CPAP has a lower treatment failure rate compared to HFNC when used as primary support; however, the indication for intubation in both groups was equivalent.

	Lavizzari *et al.* **2016**	**Roberts** *et al.* **2016**
N	316, ≥ 29 weeks GA	564, ≥ 28 weeks GA
Research design	Single-center in Italy	Multicenter in Australia and Norway
Margin	10%	10%
HFNC flow (L/min)	4 - 6 L/p	6 - 8 L/p
CPAP (cm H_2O)	4 - 6 cmH20	6 - 8 cmH20
CPAP type	SiPAP	SiPAP, Bubble, Ventilator
Outcome	Intubation and mechanical ventilation rate	Failure of primary therapy
Use of surfactant	HFNC 44.3% CPAP 46.2%	HFNC 14.4% CPAP 10.5%
	High usage rate/ low threshold	Low usage rate/ threshold not described
Rescue therapy after failure	CPAP in HFNC group upon failure	CPAP in HFNC group upon failure

1.2. Device structure and mechanism of action

The equipment providing high-flow therapy typically includes the following main components:

- Gas flow generator,

- Active respiratory gas humidification system,

- Heated breathing circuit and nasal cannula placed on the patient,

- Distilled water.

The flow generator can be an air/oxygen blender or a turbine, allowing for adjustment of the oxygen concentration (FiO2). The heated breathing circuit connects to nasal cannulas of different sizes to fit the patient's nose size.

The system delivers a blended gas mixture of oxygen/compressed air at an appropriate flow rate (typically 2 - 8 L/min for neonates), which then passes through a humidifier to warm the gas to 37°C and 100% relative humidity. The humidified gas is conducted through a heated breathing circuit to prevent heat loss and condensation in the tubing. The other end of the circuit connects to the nasal cannula attached to the patient. The nasal cannula comes in various sizes with the goal of selecting a size that ensures a leak around the nostrils is maintained.

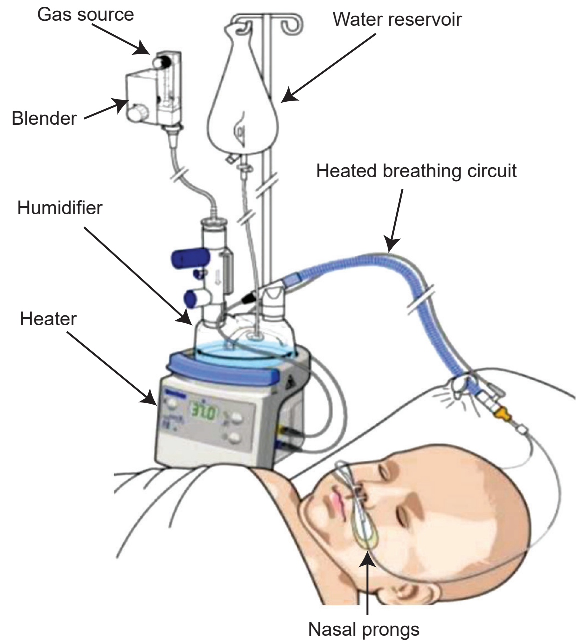

Figure 1. Main components of the high-flow system in neonates

II. HIGH-FLOW NASAL CANNULA THERAPY FOR NEONATES

2.1. Definitions

Nasal Continuous Positive Airway Pressure (nCPAP) was previously considered the standard method for non-invasive support in preterm infants.

HFNC is a form of non-invasive respiratory support using a flow of gas that has been warmed and humidified via a small nasal cannula. High-Flow Nasal Cannula (HFNC) therapy is increasingly used as an alternative respiratory support method in Neonatal Intensive Care Units (NICU) for preterm infants with respiratory pathologies.

2.2. Mechanism of action of HFNC

2.2.1. Dead space washout

HFNC washes out nasopharyngeal dead space very effectively, leading to an increased ratio of alveolar ventilation to minute ventilation (the volume of air inhaled or exhaled from the lungs per minute).

During HFNC use, the gas flow washes CO_2 out of the nasopharynx, facilitating CO_2 elimination and improving oxygenation by creating a reservoir of fresh gas in the upper airway.

2.2.2. Improvement of lung mechanics

HFNC utilizes fully humidified (100% relative humidity) and warmed gas (maintained at 34 - 37°C), which helps reduce resistance and improve lung compliance compared to using dry and cold gas. Furthermore, it improves comfort and reduces injury to the respiratory mucosa.

The use of pre-warmed and humidified gas is thought to reduce the metabolic energy that would otherwise be expended if the inhaled gas were colder or drier.

2.2.3. Reduction of work of breathing

Distension of the nasopharynx leads to higher inspiratory resistance compared to exhalation. HFNC provides a flow rate equal to or exceeding the peak inspiratory flow, thereby reducing inspiratory resistance. This means the patient does not have to exert effort to "pull" air into the lungs, as the flow is already provided.

HFNC increases inspiratory FiO2; oxygen accumulates in the nasopharyngeal cavity, creating a natural oxygen reservoir and increasing oxygen reserve function.

2.2.4. Provision of positive airway pressure

Continuous high flow generates a mild positive pressure in the airway, especially at the end of exhalation. This effect is similar to PEEP (Positive End-Expiratory Pressure) in mechanical ventilation. Providing distending pressure to the lungs helps improve ventilation mechanics by optimizing lung compliance and supports gas exchange by maintaining alveolar patency.

It is difficult to accurately measure the positive pressure due to air leaks and airway resistance. Positive pressure plays only a secondary role in the mechanism of HFNC.

2.3. Benefits of HFNC

- Less invasive.

- Reduce work of breathing by improving gas exchange.

- Reduce nasal trauma compared to CPAP.

- Provide a warmed and humidified gas stream, helping to protect the respiratory mucosa from drying and bleeding.

- Children tolerate HFNC more easily than CPAP due to lower pressure, smaller prongs, less air entering the stomach (reducing energy expenditure), and improved growth.

- Optimize parental involvement in care, including Kangaroo mother care and breastfeeding.

- Easier to establish breastfeeding. With 2 L/min, the infant can breastfeed.

- Easier nursing care with the HFNC interface.

- Lower cost than nCPAP.

- Deliver lower pressure to the lungs: reduces barotrauma and air leak syndromes (pneumothorax).

- Easier to set up and use than nCPAP.

2.4. Indications

HFNC is a non-invasive ventilation option for term and preterm infants, or used as a step-down support method from invasive mechanical ventilation or CPAP.

HFNC can be used as the primary mode of support for respiratory distress in neonates with the following conditions:

- Infants $\geq$ 30 weeks with mild to moderate respiratory distress (FiO_2 requirement < 30%).

- Apnea of prematurity.

- Post-extubation respiratory support for infants $\geq$ 28 weeks previously ventilated with MAP < 8 cmH_2O.

- Respiratory support for infants with stable Chronic Lung Disease (CLD) on CPAP (FiO_2 < 30%, P < 6 cmH_2O).

- Alternative respiratory support to NCPAP for infants with nasal septal injury from NCPAP or infants with facial defects making NCPAP application difficult.

Caution is required when applying HFNC to extreme preterm infants < 28 weeks and extremely low birth weight infants.

2.5. Limitations

- Not considered the first-line respiratory support method for patients requiring alveolar recruitment.

- Infants with severe Respiratory Distress Syndrome (RDS) requiring high oxygen with FiO_2 > 50%.

- Preterm infants < 28 weeks.

- Prolonged apnea.

- Severe hemodynamic instability.

- Pneumothorax.

- Craniofacial or airway abnormalities (choanal atresia, cleft palate, etc.).

2.6. Procedure

2.6.1. Equipment preparation

- Select an HFNC system capable of blending gas, warming, and humidifying.

- Assemble the breathing circuit according to the manufacturer's instructions.

- Fill the humidification chamber with sterile distilled water to the indicated line.

- Turn on the device and set the initial parameters:

• Temperature: 34 - 37°C.

• Relative Humidity: 100%

• Flow rate should start at 4 L/min for infants < 1 kg and 6 L/min for infants > 1 kg (maximum flow rate 6 L/min for infants < 1 kg and 8 L/min for infants ≥ 1 kg)

Current weight	Initial flow rate	Flow escalation
< 1500g	1 - 6 L/min	FiO_2 > 35% or increased respiratory rate, work of breathing
1500 - 3000g	5 - 7 L/min	
> 3000g	6 - 8 L/min	

• FiO_2: Set according to the child's previous requirements or as indicated to maintain target SpO_2.

- Allow the system to warm up completely before connecting to the child.

2.6.2. Selection and placement of cannula

- Select a nasal cannula of appropriate size for the child, ensuring there is still a gap between the prongs and the nostrils; do not completely occlude the nostrils. This ensures sufficient space for air leak, preventing excessive positive pressure buildup.

- Gently place the prongs into the child's nostrils.

- Secure the cannula using the accompanying headgear or other fixation methods, ensuring the cannula is held firmly but does not cause pressure sores on the skin.

2.6.3. Operation and monitoring

- Connect the heated breathing circuit to the child's nasal cannula.

- Keep the child's mouth open; prefer orogastric tube placement.

- Continuously monitor the child's parameters: skin color, respiratory rate, chest rise, chest retractions, SpO_2, heart rate, and blood gases (if available).

- Assess and record vital signs and work of breathing every 15 minutes during the first hour, then every hour for the next 4 hours, and subsequently every 2-4 hours once stable.

- Check the water level in humidification chambers regularly according to manufacturer regulations.

- Check that the temperature and humidity control unit is always in active status.

2.6.4. HFNC weaning

Typically, weaning from the therapy is considered in children who have been stable for 12 - 24 hours. The decision to wean HFNC is made if the child shows the following signs:

- Reduced work of breathing
- Decreased respiratory rate
- Stable blood gases.
- No apnea.
- Stable oxygen requirement.

FiO_2 should be reduced first to < 30%, then reduce the flow rate by 0.5 to 1 L/min each time, performed every 12 to 24 hours depending on the child's tolerance, based on the work of breathing.

FiO_2 > 30%	**Maintain flow rate**
FiO_2 < 25% in children ≥ 1.0kg	Reduce 1 L/min every 24 hours
FiO_2 < 25% in children < 1.0kg	Reduce 1 L/min every 48 hours
FiO_2 25 - 30%	Reduce 1 L/min every 48 hours
Requirement < 4 L/min	If the patient is breathing with FiO_2 21%, respiratory support can be stopped If FiO_2 > 21%, switch to low-flow nasal oxygen
Clinical instability Increased work of breathing Significant increase in FiO_2	Return to the previous settings and suspend HFNC weaning for at least the next 24 - 48 hours

2.7. Complications

Nasal trauma/irritation: Ensure correct cannula size and proper fixation. Use skin protection products when necessary.

Abdominal distension: May occur due to air swallowing (aerophagia). Consider gastric decompression via an orogastric tube if the condition is severe.

Pneumothorax: Although rare, high suspicion is needed if the child suddenly deteriorates.

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HFNC USAGE FLOWCHART

HFNC indications

- Non-invasive respiratory support in term/preterm infants
- Respiratory Distress Syndrome (RDS) or surfactant deficiency lung disease/grunting
- Meconium Aspiration Syndrome.
- Respiratory acidosis.
- Chronic Lung Disease.
- Apnea of prematurity.
- Post-extubation support or weaning from CPAP

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Initiate HFNC

- Start at 4 L/min for infants < 1 kg and 6 L/min for infants > 1 kg
- Select FiO_2 to maintain oxygen saturation
- Clinical assessment after 30 minutes.
- Blood gas after 2 hours.
- Flow can be increased to a maximum of 6 L/min for infants < 1 kg and 8 L/min for infants ≥ 1 kg

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Clinical improvement

Yes → Start weaning; No → Initiate HFNC

Start weaning

Start weaning	
FiO_2 > 30%	Maintain flow rate
FiO_2 <25% in children ≥ 1 kg	Reduce every 1 L/min/ 24 hours
FiO_2 <25% in children < 1 kg	Reduce every 1 L/min/ 48 hours
FiO_2 25- 30%	Reduce every 1 L/min/ 48 hours
Requirement < 4 L/min	If patient breathing with FiO_2 < 21%, stop support If FiO_2 > 21%, switch to nasal cannula oxygen
Clinical instability Increased WOB Significant FiO_2 increase	Return to previous settings and pause HFNC weaning for at least the next 24 - 48 hours.

Initiate HFNC

- CPAP
- Intubation, mechanical ventilation