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High flow nasal cannula: Mechanism of action, indications, benefits, and potential risks

Fathony Arsyad [1] and Muhammad Zulfadli Syahrul [2,*]

[1] *Residency Program in Anesthesiology and Intensive Therapy, Faculty of Medicine, Universitas Andalas, Indonesia.*
[2] *Department of Anesthesiology and Intensive Therapy, M Djamil Central General Hospital/Faculty of Medicine, Universitas Andalas, Indonesia.*

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Abstract

High Flow Nasal Cannula (HFNC) is a non-invasive oxygen therapy device with high flow that is increasingly used to treat patients with acute respiratory failure, especially in hypoxemic cases. HFNC offers several advantages, such as optimal humidification, reduced breathing work, and increased oxygenation, reducing the need for invasive mechanical ventilation. This paper aims to elucidate the mechanism of action, indications, clinical monitoring, benefits, and potential risks of HFNC use in adult patients with various clinical conditions. HFNC has various beneficial physiological effects, including increasing oxygenation by reducing anatomical dead space and producing end-expiratory positive pressure (PEEP). The main indications for HFNC include acute hypoxemic respiratory failure, post-extubation, and patients with "do not intubate" (DNI) status. In addition to its benefits, HFNC has risks, such as delayed intubation, hypercapnia, and gastric inflation, requiring close monitoring. HFNC is an effective and easily tolerated modality for treating mild to moderate acute respiratory failure. However, more research is needed to determine optimal use criteria and guidelines for therapy escalation.

Keywords: Acute respiratory failure; High flow nasal cannula (HFNC); Hypoxemic Oxygenation; Non-Invasive Oxygen Therapy

1. Introduction

Oxygen supplementation is an essential supportive therapy to maintain proper tissue oxygenation and reduce shortness of breath in patients with respiratory failure. The high-flow nasal cannula (HFNC) is a high-flow oxygen supply device increasingly used to treat respiratory failure in intensive care units (ICU). HFNC therapy is commonly used to treat acute hypoxemic respiratory failure without hypercapnia and reduce the need for tracheal intubation compared to conventional oxygen therapy (1).

HFNC has been in use for nearly 20 years, with initial research focusing on the use of HFNC in neonatal and pediatric patients, and then switched to adult application in the 2010s (2). In the pandemic, the popularity of HFNC therapy increased due to the success of the modality in hypoxemic respiratory failure. HFNC has several physiological effects, such as reduction of inspiratory resistance and work of breathing, emptying anatomical dead space in the upper airway, and mobilization of secretions by delivering oxygen-rich and humidified gases in high flow to the upper airways. In a study involving patients treated in the ICU for acute respiratory failure with coronavirus disease (COVID-19), the success rate of HFNC was 36-62% (3).

A study conducted at Hasan Sadikin Hospital Bandung from January to June 2021 on 134 patients treated in the COVID-19 isolated ICU observed the widespread use of HFNC. Among them, 44 patients were successfully weaned with HFNC,

* Corresponding author: Muhammad Zulfadli Syahrul

and 90 patients failed to wean with HFNC (4). In a study conducted at M Djamil Padang Hospital from January to November 2021, of the 299 patients who received oxygen therapy, 95 used HFNC (5).

2. Literature Review

2.1. How to use

Administered through air/oxygen blenders, heated active humidifiers, heated single-circuit, and nasal cannula, high-flow nasal cannula oxygen therapy (HFNC) is gaining increasing attention as an alternative to respiratory support for critically ill patients. The air/oxygen blender is set for FIO2 between 0.21 and 1.0 with a flow of up to 60 L/min. The gas heated and humidified by the active humidifier is passed through a heated circuit. The warm, well-moistened gas given at high flows has beneficial physiological effects. Although through open circuits, we cannot expect high final expiratory pressure (PEEP), it is reported that HFNC can create PEEP and increase the volume of the final expiratory lung (EELV) (6). The effects of PEEP vary and depend on the flow rate, the initiation of breath through the mouth or nose, the anatomy of the upper airway, and the size of the cannula against the nostril. The average PEEP value ranged from 2.7 to 7.4 cmH2O (2).

In patients with COPD exacerbations, non-invasive ventilation (NIV) has been the primary modality of choice for respiratory support because it increases tidal-inspired volume (VT) and maintains adequate alveolar ventilation. However, due to the poor tolerance of masks, NIV cannot be applied to some patients. The main difference between NIV and HFNC is in the interstitial space. While the space between NIVs increases the anatomical dead space, HFNC reduces the dead space. However, due to its open circuit, without a practical, inspirational boost or expiratory pull, HFNC cannot actively increase VT. In addition to reducing anatomical loss of space, HFNC also improves alveolar ventilation. The simplicity and excellent tolerance of the system make it even more appealing. HFNC is simple and easy to use and can reduce the use of mechanical ventilation (6).

When switching from conventional oxygen therapy to HFNC therapy, the initial settings are a flow rate of 50 liters/minute, 50% FiO2, and a dew point temperature of 37°C, also known as "50/50". The cannula's placement must be well placed in the nostrils to prevent complete occlusion. Oxygen is titrated to obtain adequate oxygen saturation, while the flow rate will be adjusted to meet the patient's inspirational flow rate needs. After starting therapy, clinical status monitoring and blood gas analysis examination should be done within 1 to 2 hours. Indications of respiratory failure, including increased work of breathing, worsening of gas exchange, and tachypnea, indicate HFNC failure and the potential need for escalation to NIV or intubation if needed (2).

2.2. Mechanism of action

2.2.1. Humidification & Mucociliary Clearance

HFNC has been shown to improve mucociliary clearance by providing moistened and heated air. Temperature and humidity suitable for human physiology (100%/37°Celsius) will provide the best conditions for mucociliary cleaning, as cilia movement works optimally at full moisture, which should be the target for long-term HFNC treatment (7).

Many high-flow nasal cannula systems are designed with inline heating and humidification systems that provide air with appropriate humidity and body temperature that does not irritate the mucosa, increasing patient comfort (31 to 37°C). Thus, heated and humidified oxygen can improve clearance of secretions, reduce airway inflammation, increase comfort, lead to better compliance, and minimize energy expenditure, especially in acute respiratory failure. In addition, HFNC also prevents bronchoconstriction or bronchospasm caused by dry and cold air, which improves patient comfort and tolerance (8,9,10).

2.2.2. Anatomical Dead Space Flushing

The high flow rate in HFNC therapy provides an air volume that exceeds the patient's physiological ventilation, improving ventilation and replacing excess CO2 with excess O2. It increases PAO2, creates a more significant oxygen diffusion gradient, and potentially improves patient oxygenation. HFNC has been shown to reduce trans-diaphragmatic pressure, which is a measure of inspirational effort and work of breathing. Although the positive end-expiratory pressure (PEEP) effects of HFNC are minimal, this therapy is effective enough to overcome hyperinflation in patients with COPD and thus also reduce the expiratory workload. In addition, better ventilation also contributes to the stabilization of oxygenation, which is driven by changes in anatomical dead space and alveolar recruitment (7,11).

2.2.3. Increased Inspiration Flow and Fraction of Oxygen (FIO2)

At flows of 1–6 L/min, FIO2 ranges from 0.26 to 0.54 during calm breathing and 0.24 to 0.45 during rapid breathing, increasing to 0.54–0.75 and 0.49–0.72 at flows of 6–15 L/min. FIO2 is higher when breathing with the mouth open than when breathing with the mouth closed (6). Patients with acute hypoxia can have a peak inspiratory flow of between 30 to 120 L/min, while conventional oxygen therapy can only provide a flow of up to 15 L/min. HFNC can meet the oxygen flow needs of patients with respiratory failure, so the inspired oxygen volume fraction remains constant and reaches the patient's needs (up to 90% of the oxygen volume fraction can be achieved). HFNC can provide oxygen concentrations between 21% to 100% and oxygen flow of up to 60 L/min, which can meet the needs of patients with acute hypoxia. The flow of oxygen administered approaches or even exceeds the spontaneous inhalation of patients with respiratory failure (9).

2.2.4. Positive end-expiratory pressure (PEEP)

HFNC exerts positive end-expiratory pressure (PEEP) in the lower respiratory tract. This effect is similar to continuous positive airway pressure (CPAP), which applies a supportive force to prevent the alveolar duct from collapsing under the increased surface strain pressure during expiration. Patients should keep their mouths closed to get the maximum benefit of PEEP from HFNC. The approximate PEEP produced with the mouth closed is about 1 cm of water pressure for a 10-liter flow. There was an increase in the final volume of expiration along with the increase in PEEP (9).

2.2.5. Interface

HFNC nasal prongs are softer and more flexible than conventional nasal canuls and face masks. Available in small, medium, and large sizes for adults. Choosing a size that maximizes the ratio between the nasal prongs and the nares is important, as this affects the positive pressure channeled into the airways without negatively affecting breathing difficulties or comfort. HFNC can also be delivered via tracheostomy (provided the patient does not require mechanical ventilation), which can be performed in a hospital or at home using a commercially available adapter (10).10

2.2.6. HFNC indications

1. Acute hypoxemic respiratory failure (mainly due to community-acquired pneumonia)
2. Post-extubation
3. Pre-intubation oxygenation
4. Acute hypercapnic respiratory failure
5. Do not resuscitate (DNR)/do not intubate (DNI) in respiratory distress
6. Cardiogenic pulmonary edema
7. Acute heart failure
8. Sleep apnea

2.2.7. HFNC usage monitoring

Clinical monitoring of patients using HFNC is carried out at least within 30 minutes in the first 1 hour, then every hour. Several clinical parameters are significant prognostic factors for HFNC failure, so monitoring them, including respiratory rate, SaO2, SpO2, blood gas analysis, and ROX index (ratio of SpO2/FiO2 to respiratory rate) is necessary.

$$\mathrm{ROX} = \frac{\mathrm{SpO2/FiO2}}{\mathrm{Respiratory\ Rate}}$$

Within 1-2 hours after the initiation of HFNC, several respiratory parameters that are adverse prognostic factors need to be examined, such as respiratory rate 35x/min, asynchronous thoracoabdominal movements, and the use of breathing support muscles. Any of these parameters indicates that the patient does not respond immediately to HFNC; a short-term non-invasive ventilation experiment may be considered before intubating the patient. If none of these parameters are present, then HFNC can be continued, and initial arrangements need to be titrated based on the patient's respiratory rate and SpO2 (88-90%) and the patient's comfort and tolerance. HFNC settings need to be checked and adjusted during patient monitoring.

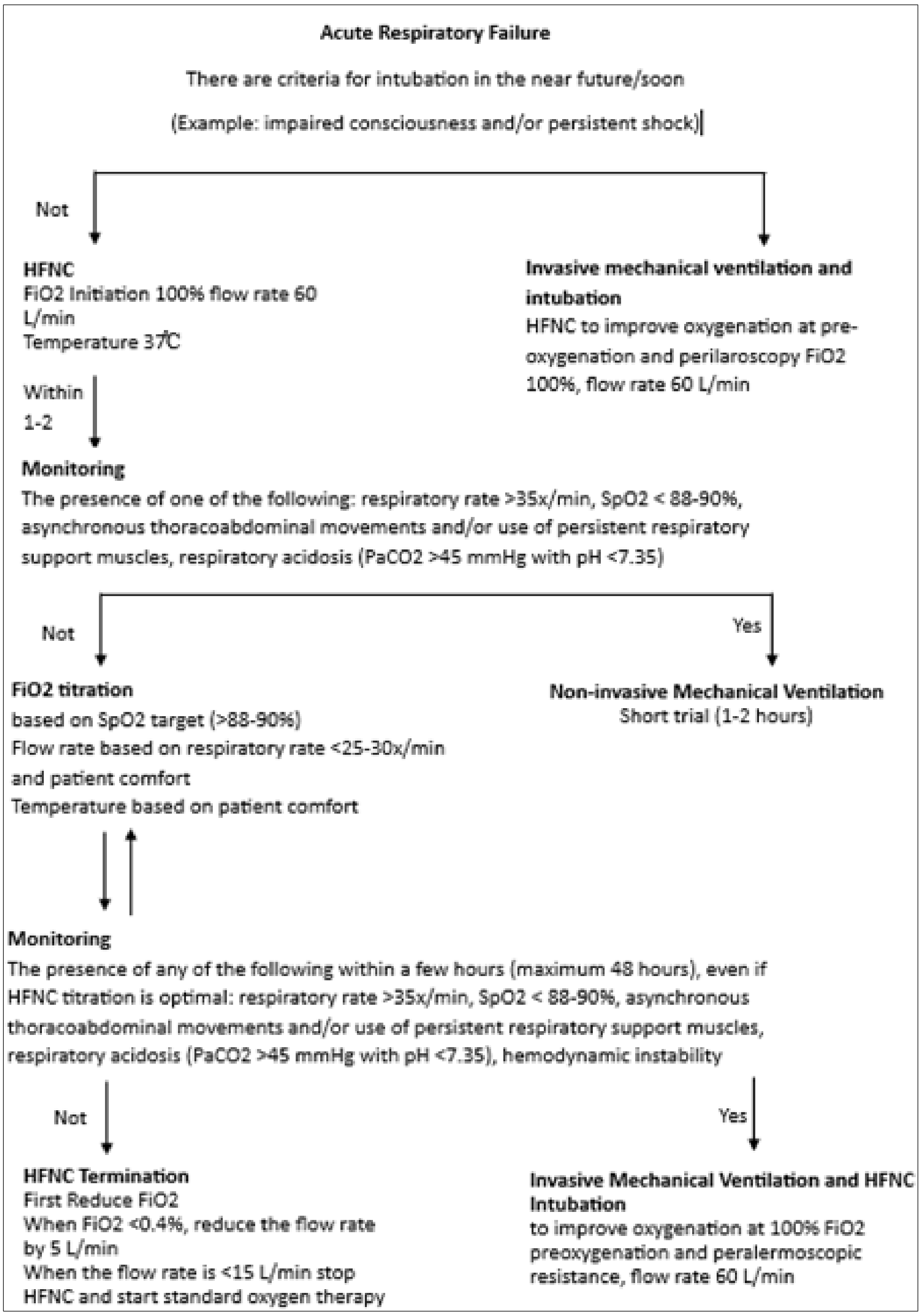

Figure 1 HFNC oxygen therapy algorithm in acute respiratory failure (12)

The ROX index can help clinicians to predict HFNC failures. ROX index values of <2.85, <3.47, and <3.85 in the first 2, 6, and 12 hours of HFNC use constitute HFNC failures. However, the overall clinical assessment is undoubtedly still better. The application of the ROX index for specific cases such as COVID-19 is still under further study.

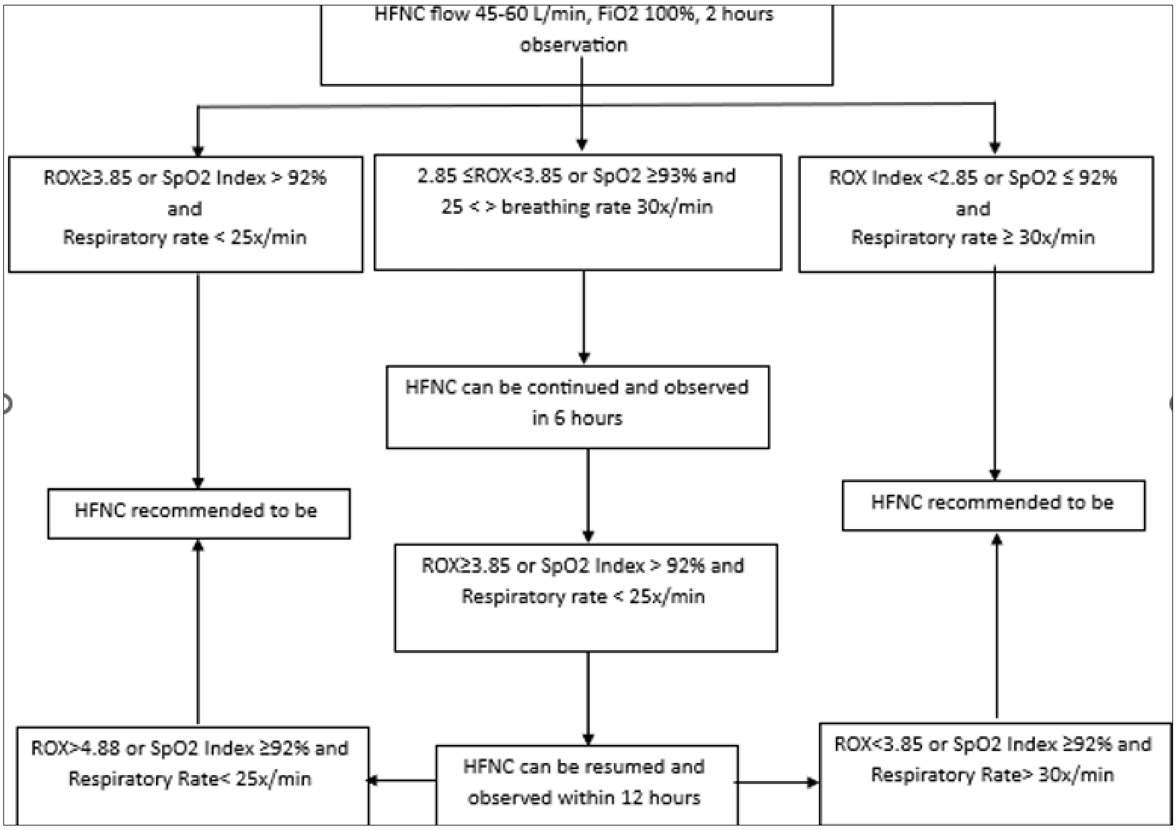

Figure 2 HFNC usage guide using ROX (12)

Close monitoring in patients with HFNC is essential to prevent unwanted respiratory and cardiac complications, especially in the first 48 hours. In addition to the parameters mentioned above, other parameters such as hemodynamic instability (heart rate >140x/min or change >20% of baseline value and/or systolic blood pressure >180 mmHg, 40 mmHg from baseline value). If the patient does not improve within 48 hours, HFNC therapy is declared to have failed, and invasive mechanical intubation and ventilation are necessary as soon as possible.

Discontinuation of HFNC and initiation of intubation and mechanical ventilation is based on clinical judgment from the primary care physician, guided by protocol recommendations to consider mechanical ventilation in the presence of persistent/worsening respiratory distress, respiratory rate >40 times/min, SpO2 < 90% for more than 5 minutes despite maximum current and FiO2, acidemia with pH < 7.35, significant hemodynamic instability (defined as systolic blood pressure <90 mmHg, mean arterial pressure <65 mmHg or vasopressor need), decreased neurological status (GCS <12) or inability to clear airway secretions. Some studies have stated that if the patient does not improve within 48 hours, HFNC therapy is declared to be a failure, and it is necessary to undergo invasive mechanical intubation and ventilation as soon as possible. Maintaining failed HFNC therapy can mask further respiratory damage and increase mortality rates. If the patient's clinical and gasometric parameters improve gradually, then FiO2 must be gradually lowered, followed by a gradual decrease in current by 5-10 L every 15-30 minutes. The interval of these two decreases is adjusted to the clinical and physiological parameters of the patient. When the patient is stable for 1-2 hours with 40% FiO2 and a current of 15-20 L/min, HFNC oxygen therapy can be discontinued, and conventional oxygen therapy can be started (12).

2.3. Advantage

2.3.1. Comparison with NIV

Currently, there are no high-quality controlled studies that are HFNC and NIV. However, several previous studies have provided some insight into the effectiveness of both methods. In a case study, it was reported that five patients with moderate (20%) to severe (80%) dyspnea in patients with Acute Heart Failure (AHF) who initially did not show a good response to NIV in the emergency room were transferred to HFNC. As a result, significant improvements occurred in dyspnea and patient comfort. After 24 hours of HFNC therapy, the SpO2 of the patient's arteries increased from 85% to 99% (9).

2.3.2. Comparison with Conservative Oxygen Therapy

HFNC is a good alternative to traditional oxygen therapy in patients with mild to moderate hypoxemia. Rochwerg et al., through meta-analysis of HFNC research in recent years, showed that in patients with respiratory failure. However, HFNC did not affect mortality; HFNC reduced the need for invasive mechanical ventilation (RR 0.85, 95% CI 0.74-0.99) and reduced absolute risk by 4.4% compared to conventional oxygen therapy. Zhu et al. showed that compared to traditional oxygen therapy, HFNC minimizes the need for increased respiratory support and can be safely used in patients after adult heart surgery (9).

2.4. Disadvantages

2.4.1. Intubation Delay in HFNC Failure

The main complication most common in using HFNC is the delay in intubation when HFNC oxygen therapy fails to provide clinical improvement in the patient. One study found that HFNC use more than 48 hours before intubation was associated with higher mortality rates in intensive care units, reduced success in extubation and ventilator release, and lower ventilator-free days. Another study showed that patients who underwent invasive mechanical intubation and ventilation after HFNC had a significantly higher mortality rate than patients who underwent immediate invasive mechanical intubation and ventilation without HFNC (12).

2.4.2. Pneumothorax and Pneumomediastinum

Complications of pneumothorax and pneumomediastinum can occur in the case of children. In these cases, oxygen administration was reported to exceed the recommended protocol (12).

2.4.3. Hypercapnia

In the use of HFNC for apneic oxygenation, one potential complication is hypercapnia. A study showed that the partial pressure of carbon dioxide ($PaCO_2$) increased by three mmHg/min during apneic oxygenation via HFNC at a current of 50 L/min. $PaCO_2$ was significantly higher in apnea with HFNC compared to bag-mask ventilation. Still, the resultant increase in $PaCO_2$ in HFNC appeared tolerable because the highest $PaCO_2$ level was estimated to be 65 mmHg after the completion of tracheal intubation (12).

2.4.4. Gastric Inflation

Gastric insufflation (air entry into the stomach) is a theoretical complication due to HFNC because HFNC creates positive airway pressure. An increase in current of 10 L/min is known to cause an increase in nasopharyngeal airway pressure by 1.2 cmH_2O (12).

3. Conclusion

Oxygen delivery via HFNC has proven to be an effective method of noninvasive ventilation support. It is gaining increasing attention as a simple and easily tolerated alternative to respiratory support in critically ill patients. Doctors have used HFNC for various underlying diseases and conditions, and it appears to be effective in treating hypercapnic respiratory failure and mild to moderate hypoxemic respiratory failure.

However, more rigorous evidence is still needed to establish some essential criteria, such as indications for the use of HFNC, criteria for initiating and discontinuing them, and indications for escalation of treatment. Because HFNC is non-invasive, PEEP or CPAP is not measured. Despite some of these problems, growing evidence suggests that HFNC is an effective modality for the initial treatment of adult patients with respiratory failure associated with a variety of underlying diseases.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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