Chapter

High-Flow Nasal Cannula

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Abstract

Conventionally, oxygen is given at 4 to 6 L/min through nasal cannula for supplementation of oxygen. The FiO_2 achieved through this can be up to 0.4. Flows more than this can cause dryness to the nasal mucosa without much increase in the FiO_2. High-flow nasal cannula (HFNC) uses flow up to 60 L/min. Positive end-expiratory pressure is created in the nasopharynx and it is also conducted to the lower airways. Studies have shown HFNC improves washout of CO2 and decreases respiratory rate. Patient compliance also improves due to the comfort of the cannula compared to the non-invasive ventilation through a mask.

Keywords: non-invasive ventilation, high-flow nasal cannula, positive end-expiratory pressure, humidification

1. Introduction

Typically, respiratory support devices fit into three major categories: conventional oxygen delivery devices, non-invasive respiratory support, and invasive respiratory support. High-flow nasal cannula (HFNC) comes under a new category between conventional oxygen delivery device and non-invasive respiratory support. High-flow oxygen *via* non-rebreather mask can supplement oxygen at high concentration, provided the flow is around 10–15 L/min. At this rate, the medical gas is not humidified efficiently and this unwarmed and dry gas causes mask discomfort, and eye, oral, and nasal irritation [1]. Non-invasive ventilation is conventionally administered with a tight-sealing face mask, which might cause discomfort to the patient. Hence, it is associated with poor compliance when compared to other oxygen delivery systems. A device with better compliance with some added advantages of positive end-expiratory pressure (PEEP) and humidification would be a blessing to the patients and the caregivers.

In 1987, for the first time, oxygen therapy at a maximum flow rate of 20 L/min, with heated humidification system, was used in oxygen therapy for patients with bronchiectasis and cystic pulmonary fibrosis to promote the removal of lower respiratory tract secretions. It is still being extensively studied in respiratory distress syndrome, in apnea of prematurity in the neonate and pediatric units [2]. In adults, it has been used to treat acute respiratory failure, high-risk extubations in ICU, and many other clinical scenarios.

2. Mechanism

HFNC has an air/oxygen blender, which delivers the gas at desired FiO_2 regardless of the flow rate. The heated humidifier is an inline system and actively humidifies the inspiratory gas. Other conventional oxygen therapy (COT) devices mostly through bubble humidification deliver non-humidified or under-humidified gas to the patient. Additionally, the nasal cannula of HFNC differs from the conventionally used nasal prongs by being loose, larger, and softer, which improves tolerance (**Figure 1**).

2.1 Mucociliary clearance and humidification

Epithelial cells of the respiratory tract when exposed to dry gas for 4 to 8 h have been shown to have reduced function and increased inflammation. The mucociliary clearance was studied with saccharin transit times, and there was 40% delay in the transit when patients were supplemented with dry non-humidified or under-humidified oxygen. Hence, adequate humidification is vital in maintaining the functions of respiratory epithelial cells [3]. Breathing unwarmed dry gas can increase resistance and decrease pulmonary compliance as well [4]. This is also partly attributed to receptors in the nasal mucosa, which results in muscarinic receptors-mediated bronchoconstriction in the lower airways [5].

During spontaneous breathing of room air, humidification is actively done by the nasal mucosa and nasopharynx. As per Dalton's law, the warmer the gas, the more water vapor is held. In this process of heating, some energy expenditure occurs in the human body. Supplementation of heated and humidified air reduces energy expenditure and can reduce CO2 production and decrease oxygen consumption. This mechanism is also supported by the study in infants, which showed increased weight gain in patients treated with HFNC [6, 7].

2.2 Washout of dead space

About 30% of the tidal volume does not participate in gas exchange. This is due to the anatomical dead space from the nose to the terminal bronchiole. The volume of this dead space is fixed and when the tidal volume reduces, the proportion of dead space ventilation increases. The effect of this dead space is higher in shallow breathing in a patient with respiratory insufficiency. In acute respiratory distress syndrome (ARDS), this dead space ventilation can go above 60% above the tidal volume (i.e., $V_D/V_T \geq 0.6$) [8]. In a spontaneously breathing patient, HFNC

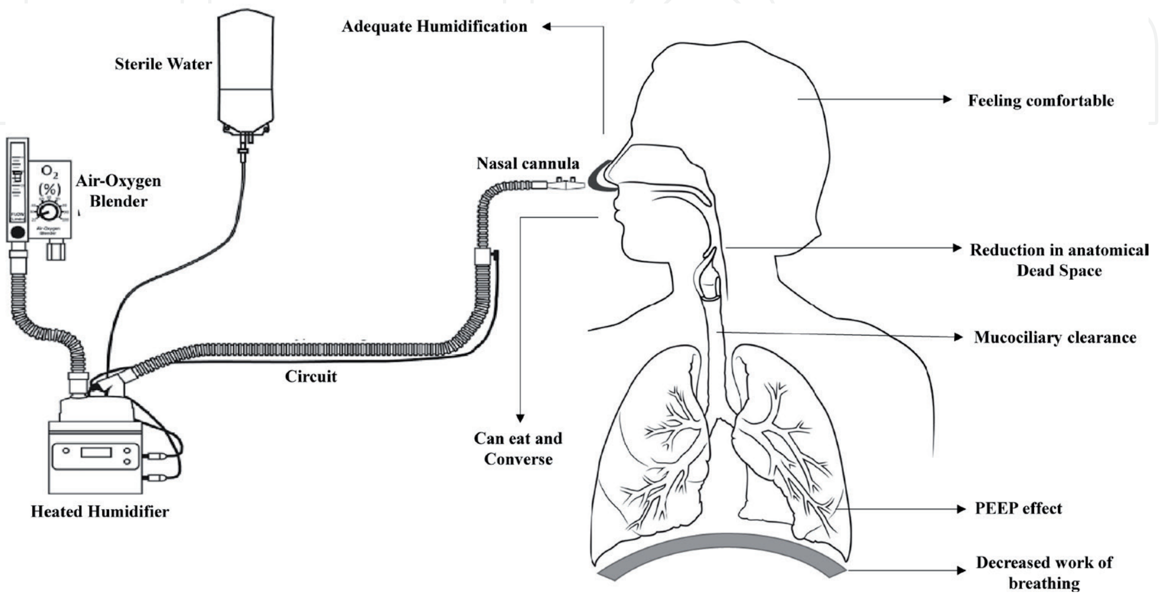

Figure 1.
Components and effects of HFNC.

washes out the exhaled gas in the nasopharynx and replaces this dead space with a lower CO2 and higher oxygen air mixture, and this oxygen-rich air is breathed in by the patient at the next cycle, which helps in washing out the CO2. It was evident by the reduction in minute ventilation at a constant arterial CO2 tension and pH, in the studies [9].

2.3 Patient acceptance

Non-invasive ventilation (NIV) has a low acceptance rate from the patient point of view due to the discomfort of tight-fitting mask and variable levels of humidification according to the type of humidification used. Studies have shown that HFNC is better tolerated than NIV [10]. Also, when compared with face mask (FM), oxygen supplementation with a bubble humidifier HFNC is shown to be better tolerated. In a study involving oxygen supplementation at 15 L/min through FM with bubble humidifier and HFNC, patients on HFNC had greater overall comfort level, lower dyspnea scores, and reduced mouth dryness [11].

In "do not intubate" scenario, there is no change in outcome observed between NIV and HFNC, but the patients who were on HFNC had better diet intake, who conversed until just before their death. People like to eat by themselves and to talk with their friends and family at the end of their life, and HFNC favored patients in these requirements [12].

2.4 Work of breathing

The peak inspiratory flow in patients with respiratory failure is around 60 L/min and HFNC can match this flow, when compared with COT devices, and hence helps in reducing the work of breathing during the inspiration. The reduction in work of breathing was also evident in the form of lower inspiratory esophageal pressure swing, better compliance ($V_t/\Delta Pes$), and lower PTP and PTP_{min} in HFNC group compared with face mask and oxygen [9].

2.5 PEEP effect

At higher flow rates through the nasal cannula, positive pressure is created in the nasopharynx. The effect of positive pressure is higher when the patient is breathing with the mouth closed as it creates a seal. Some amount of airway pressure is lost if the patient opens the mouth.

The mean pressure generated with flows between 10 and 15 L/min was 1.7 to 5.3 cm H_2O. Anatomical differences in the nares' size and variability in the airway among the patients, varying leak around the bores of the HFNC, might have led to this wide variation in the pressure created in the airway [13]. The positive pressure created in the airway is maximum at the end of expiration. For each increase of 10 L/min of flow, there is an increase in mean airway pressure of 0.69 cm H_2O, in patients breathing with mouth closed. It decreases to 0.35 cm H_2O if the patient is breathing with mouth open [14]. These studies have measured the pressure changes by placing a catheter through the nasopharynx and placing the tip of the catheter at the level of uvula. Whether this pressure created in the nasopharynx is conducted down to the respiratory system is the next question. There is an increase in functional residual capacity when electrical impedance tomography is used to study the effect of HFNC. The pressure created in the nasopharynx by the high flow is transmitted down to the lower airways and there is an increase in the lung volume. The increase in lung volume is much homogenous in the prone position when compared to supine position. In the supine position, the expansion of lung is predominant in the ventral region [15].

3. Clinical use

3.1 Difficult intubation

In case of difficult intubation, HFNC can be given to patients as a method of pre-oxygenation and can be continued during induction, relaxation, and laryngoscopy. Clinicians should note that a jaw thrust is necessary to keep the airway in continuum with the nasopharynx. This method is called Trans-nasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE), which has improved the apneic time up to 17 min with $PaCO_2$ levels around 60–75 mm Hg [16]. It is a potential alternative to high-flow intra-tracheal oxygen insufflation for apneic oxygenation. Patients could maintain oxygen saturations for a longer time during the apneic oxygenation and this could change the nature of difficult intubations from a hurried stop-start event to a smooth event.

3.2 Hypoxemia

The mechanisms of action of HFNC and its comfort make it a first-line oxygen delivery device for adult patients with hypoxemia. The beneficial effects of HFNC are evident by reduction in respiratory rate and improvement in oxygen saturation [17]. It not only improves the numbers in arterial blood gas, but also improves the patient clinically in terms of dyspnea score, supraclavicular retraction, and thoraco-abdominal asynchrony. All these benefits can be seen as early as 15–30 min [18]. When compared with COT devices, HFNC has shown to have reduced requirement of NIV for rescue [19].

However, the results were not the same in other studies. In a study involving patients presenting with respiratory failure to the emergency department, HFNC was not superior to COT devices in terms of escalation to mechanical ventilation, length of hospital stay, and 90-day mortality. Similar results were seen in FLORALI trial, except for reduced mortality at 90 days in patients treated with HFNC [20]. Authors attributed this benefit to degree of comfort, the heating and humidification of inspired gases, which prevented thick secretions, low levels of PEEP generated by a high gas flow rate, and reduction in dead space.

In a meta-analysis, authors concluded that, in hypoxemic patients with respiratory distress, HFNC was not better than COT devices in terms of mortality, but when compared with initiation of mechanical ventilation and escalation of therapy, HFNC was associated with risk reduction [21]. In immunocompromised patients with respiratory failure, HFNC was associated with reduction in the rate of intubation and mechanical ventilation when compared with the COT devices and NIV [22]. HFNC is also useful in treating patients with stable hypercapnic COPD and obstructive sleep apnea [23, 24].

3.3 Extubation in ICU

Extubation in intensive care unit is associated with 12–14% of re-intubation mostly within 72 h. NIV is advised in high-risk patients to prevent early re-intubation [25]. HFNC can be an alternative to NIV in patients with high risk of re-intubation. However, the results were contradictory. Compared with conventional oxygen delivery devices, HFNC has reduced the incidence of re-intubation in high-risk patients in few studies and it has not, in few other studies [26–29].

3.4 Postoperative management

In cardiothoracic postoperative patients, HFNC is equal to NIV in preventing postoperative pulmonary complications. Patients treated with HFNC and NIV had similar rates of treatment failure and mortality. But for the ease of nursing care and better acceptance from the patients, HFNC can be an alternative to NIV in postoperative cardiac surgeries [30]. In case of major abdominal surgeries, the incidence of hypoxemia in the postoperative period is 10–50% according to various studies. Pulmonary complications are due to loss of functional alveolar units because of de-recruitment and basal atelectasis. In this subset of postoperative patients, HFNC was inferior to NIV in preventing hypoxemia and in terms of length of stay [29].

3.5 Pediatrics

There is a lack of guidance of flow in the pediatric population. About 1–2 L/min, for less than 24 months, is advised and sometimes a flow of 0.5 L/min is used in neonates. Regarding cannula size for the pediatric patients, the manufacturers recommend that the cross-sectional area of the cannula should not be more than 50% of the cross-sectional area of the nares and the outer diameter of the cannula should not be more than two-thirds than that of the nares. Discrepancies in size might lead to unexpected elevations in airway pressure or excess air leak.

In optimum conditions, the pressure created by the HFNC is comparable to nasal CPAP. But with increasing leak, the pressure effect diminishes and varies between patients. A pressure release valve is necessary in neonatal HFNC as the flow is fixed and directly delivered to the infant, to prevent over distension and injury [31]. In a retrospective study involving premature infants with neonatal respiratory disease, there were no differences in incidence of bronchopulmonary dysplasia, and no difference in rate of infection and death. But more infants were intubated for failing early nasal CPAP compared with early HFNC [32]. In another study involving nasal CPAP and HFNC as a prophylaxis to prevent re-intubation in high-risk preterm infants, HFNC failed to maintain the extubation status of the preterm infants [33]. When compared with COT, HFNC has shown to reduce extubation failures in pediatric population [34].

In addition to respiratory failure, post-extubation, and pre-oxygenation, acute bronchiolitis is the main indication for HFNC in pediatric patients. In studies, there were no differences in length of stay, intubation rate, respiratory rate (RR), SpO_2, or adverse events in patients treated with HFNC versus COT devices and nasal CPAP groups. But treatment failure was higher in the HFNC group when compared with nasal CPAP group and lower in the HFNC group when compared with COT devices group [35]. In status asthmaticus, HFNC when compared with COT devices had better pCO_2 levels, pH, improvement in SpO2, and reduction in respiratory rate [36]. In children who do not tolerate CPAP for OSA, HFNC has proved to be a better alternative. In a study involving children not tolerating CPAP, use of HFNC has reduced obstructive apnea-hypopnea index by 9 events/h and desaturation episodes by 13 events/h on an average [37]. HFNC stands between COT devices and CPAP in bronchiolitis and for prophylaxis after extubation. Better designed, larger studies are needed for other indications and comparisons with other oxygen delivery and ventilating systems.

3.6 Initiation and titration

In a patient with acute respiratory distress, first the eligibility of the patient for non-invasive support is to be assessed. Whoever it does not fit in the criteria should be intubated to protect the upper airway and mechanical ventilated. Patients who can be given a trial of HFNC are started at 40 L/min flow, 100% FiO_2, and 31°C temperature. Temperature of 31°C is more comfortable to patients than temperature of 37°C. FiO_2 is titrated down for a SpO_2 target of 90%. Patient is assessed after 1–2 h and in case of respiratory rate > 35/min or the FiO_2 requirement is more than

45%; then, the flow is increased by 5–10 L/min. Once the maximum recommended flow of 60 L/min is reached, FiO_2 is gradually increased for the desired targets. The targets are SpO_2 just above 90% and respiratory rate less than 35/min (**Figure 2**).

In case of clinical improvement, first the FiO_2 is titrated down to 40–50%, and then, the flow is titrated down 5–10 L/min per session. The frequency at which the flow is adjusted depends on the clinical situation. Once the flow reaches less than 20 L/min, the patient can be weaned from HFNC and can be put on COT devices [38].

HFNC is being attributed to delay in intubation and studies have shown increased mortality in such situations. Failure of HFNC might cause delayed intubation and worse clinical outcomes in patients with respiratory failure [39]. Roca et al. derived an index to predict the success of HFNC in patients with respiratory failure and pneumonia. ROX (Respiratory rate – OXygenation) index with oxygenation as numerator (SpO_2/FiO_2 ratio) and respiratory rate as denominator is calculated after 12 h of initiation of HFNC therapy. A value less than 4.88 identified patients who will fail HFNC and require intubation (area under curve of 0.74; 95% CI, 0.64–0.84) [40]. This index was also externally validated, and their calculated cutoff was 3.85. A score of more than 4.88 suggests therapeutic success of HFNC and a score of less than 3.85 is suggestive of failure of HFNC and needs intubation as delayed intubation is associated with poor outcomes. There is a gray area between 3.85 and 4.88. In that case, ROX index to be calculated after 1–2 h and in case if it is increasing, then invasive mechanical ventilation is recommended (**Figure 3**).

3.7 Adverse effects

HFNC is more expensive than COT devices and that limits its widespread use. When compared with COT devices and NIV, administration of HFNC is considered as an aerosol-generating procedure. This might put the health care workers at risk and in case of a communicable disease, this will be an additional burden during an epidemic or a pandemic. The aerosol dispersion can be up to 17 cm from the patient, with the use of HFNC at 60 L/min. This dispersion is higher than the simple face mask delivering oxygen at 6 L/min, but it is lesser than the devices that deliver higher flows such as non-rebreathing face mask (24 cm) and venturi mask (39 cm) [41, 42]. Clinician should make sure the fit and seal of the HFNC is satisfactory, or else the lateral spread of aerosol can be as high as 60 cm in case the interface is loose. In another study involving patients with bacterial pneumonia, who were either on HFNC or on face mask, with settle plates at 0.4 and 1.5 meters from

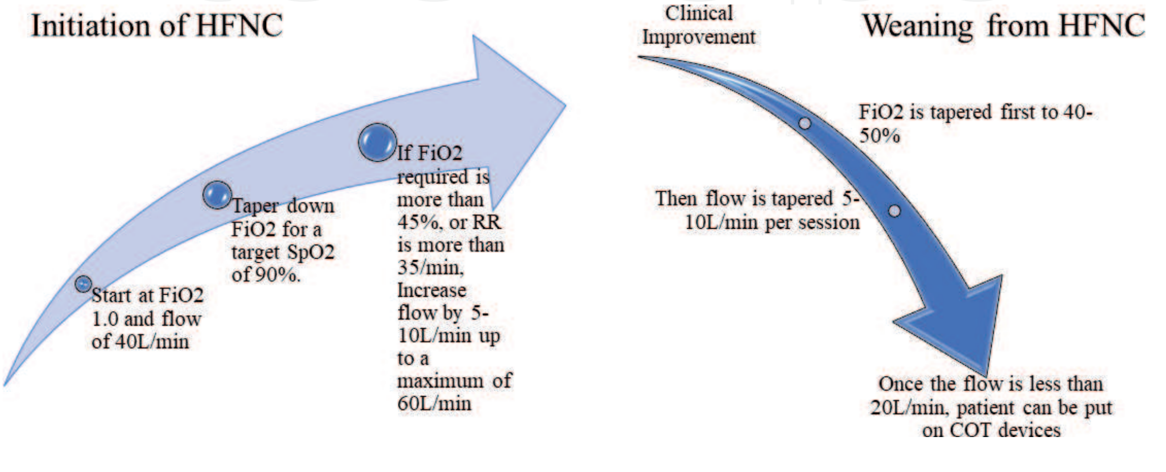

Figure 2.
Initiation and titration of HFNC. FiO2—Fraction of inspired oxygen. SpO2—oxygen saturation in blood. RR—respiratory rate. COT—Conventional oxygen therapy (Adapted from Ischaki et al. [38]).

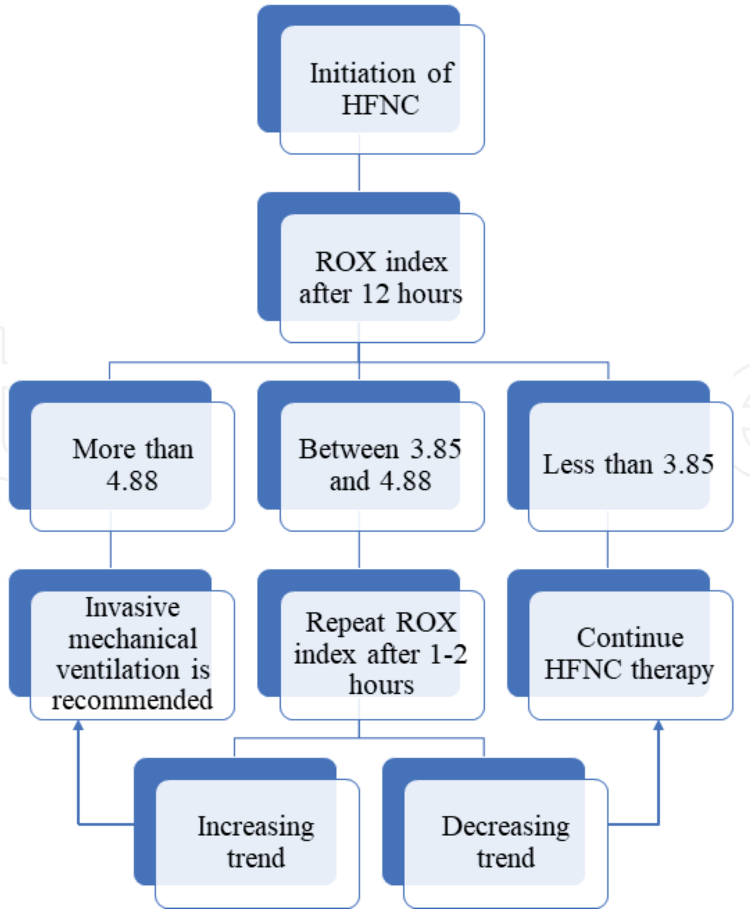

Figure 3.
Utility of ROX index. ROX—Respiratory rate-OXygenation (adapted from Roca and Messika et al. [40]).

patients, there was no significant difference in bacterial counts in the air sample between HFNC and face mask [43]. Even though studies do not establish transmission of disease through HFNC, there is uncertainty and fear of aerosol dispersion [44, 45]. Addition of a surgical mask over the HFNC can prevent aerosolization, which is not possible in case of oxygen face masks [46].

Similar to NIV, HFNC also has the potential for delaying intubation when clinically indicated. Patients who got invasively ventilated after 48 h of NIV had higher mortality than those intubated and ventilated within 48-h therapy. Hence, early detection of NIV/HFNC failure is vital for optimum management [38].

One of the beneficial effects of HFNC is the positive pressure created in the airway, but that can be maximum up to 7 cm H_2O and there is loss of positive pressure if the patient opens the mouth [14]. When compared with COT devices, HFNC had higher PaO_2, but the effect was attributed to higher FiO_2 achieved as the PF ratio was unaffected. But when compared with HFNC, NIV not only had higher PaO_2, but also higher PF ratio, which was attributed to its higher PEEP effect. The peak inspiratory flow generated by patients with respiratory failure is around 60 L/min, which can increase further, when there can be entrapment of room air, which will affect the FiO_2 achieved, whereas the FiO_2 delivered to the patient using NIV can reach 100% with proper seal and the higher flow demand of the patient is also matched by the ventilator.

3.8 Complications

Prolonged use of HFNC may lead to abdominal distension, aspiration, and barotrauma, although the risk of barotrauma is much less as compared with non-invasive or mechanical ventilation. A well-known complication of HFNC is barotrauma such as air trapping, pneumothorax, and pneumomediastinum. The equipment is costlier and involves more technology and accessories than conventional nasal cannula. There is a learning curve for the caregivers but that is usually quickly achieved.

3.9 Contraindications

HFNC is contraindicated in patients who are unresponsive or agitated and patients at risk of aspiration. HFNC will be of limited use in patients with airway obstruction due to tumors. Facial anomalies, recent or past facial surgery, or facial trauma might hinder the use of HFNC. It is better avoided in patients with upper airway surgery to avoid the theoretical risk of venous thromboembolism due to the high pressure during its use.

4. Conclusion

HFNC lies in between conventional oxygen delivery devices and NIV. HFNC has been used to treat hypoxemic respiratory failure, cardiogenic pulmonary edema, and post-extubation prophylaxis to decrease pulmonary complications, and in high-risk extubations. However, most of the studies addressing these are of low quality to draw conclusions and strong recommendations. HFNC can be of useful value in a setup where there is continuous monitoring of patients.

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