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High-flow oxygen therapy — its application in COVID-19-related respiratory failure and beyond

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ABSTRACT

Oxygen therapy is the primary method of treating acute respiratory failure during Sars-CoV-2 infection. Depending on the patient's condition, treatment may be carried out using traditional nasal cannulas, oxygen masks, non-invasive ventilation or mechanical ventilation. A relatively modern method that has been used worldwide for about 10 years is High Flow Nasal Oxygen Therapy (HFNOT). Equipment for HFNOT allows you to obtain high (up to 60 L/min) flows in nasal cannulas and precisely set a high concentration of oxygen in the mixture of inhaled gases. Such high flow is also associated with the generation of constant positive pressure in the airways, which further supports the treatment of respiratory failure by maintaining airway patency, recruitment of alveoli and reducing the breathing workload. HFNOT also leads to a reduction in anatomical dead space and facilitates carbon dioxide washout from the upper respiratory tract which also reduces the work of breathing and increases the efficiency of ventilation.

Moreover, this ventilation method is tolerated well by patients and does not require specialized and long-term personnel training. Therefore, the method was widely applied in hospital wards treating patients with severe respiratory failure during Coronavirus Disease 2019 (COVID-19). Additional applications for this relatively novel method of oxygen support in different fields of medicine were analysed.

Keywords: high-flow nasal cannula, high-flow oxygen therapy, HFNC, HFNOT, COVID-19, Sars-CoV-2, acute hypoxemic respiratory failure

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Introduction

Sars-CoV-2 is the novel human coronavirus responsible for the COVID-19 pandemic. One of the main complications of the disease includes pneumonia and acute respiratory distress syndrome [1]. Previous reports show that the development of acute respiratory distress syndrome (ARDS) occurs in 3–20% of patients requiring hospitalization due to COVID-19 and in more than 60% of patients whose condition at the time of diagnosis was classified as critical [2].

Methods of non-invasive support of ventilation in patients with acute hypoxemic respiratory failure in the course of COVID-19 remain a topic of debate. Many medical studies point to the use of High Flow Nasal Oxygen Therapy (HFNOT) devices as an effective and well-tolerated method of respiratory support in patients with moderate and severe respiratory failure [3, 4]. Considering the above, high-flow oxygen therapy may prove to be an effective support in the treatment of pneumonia in patients with COVID-19. The following paper describes the mechanism of HFNOT's action, its role in patients with acute respiratory failure, its advantage over conventional oxygen therapy and a comparison of high-flow oxygen therapy with non-invasive ventilation. Moreover, additional applications for its use in other fields of medicine were analysed.

HFNOT: an introductory insight

HFNOT systems allow you to obtain high (up to 60 l/ /min) flows in the nasal cannula and precisely set and control the concentration of oxygen in the mixture of inhaled gases (fraction of inspired oxygen [FiO_2] from 21 to 100%). The breathing mixture administered to the patient is moistened (up to 44 mg H_2O/L) and heated to the temperature selected by the operator (within 34–38 °C) [5].

HFNOT requires specialized equipment: an oxygen mixer, a gas flow generator and a system for heating and humidifying them. The equipment also includes disposable tubing systems, dual-lumen nasal cannulas (available in several sizes; possibly with specially designed adapters for the use of HFNOT on tracheostomy patients), and a fluid reservoir to moisturize the respiratory mixture. Currently, the market is dominated by two types of devices that enable the implementation of the HFNOT technique: Precision Flow (Vapotherm) and Optiflow (Fisher & Paykel Healthcare Ltd.) [6].

HFNOT: the mechanism of action

The high gas flow associated with the high-flow nasal cannula removes the expiratory air from the upper airways in favour of the delivered breathing mix, reducing the dead space in the upper airway, and thereby increasing alveolar ventilation [7].

The high-flow nasal cannula reduces the resistance of the nasopharyngeal airways leading to improved ventilation and oxygenation through the use of a positive-pressure environment. This results in a reduction in breathing effort, which facilitates slow and deep breathing [8].

In addition to providing positive pressure in the nasopharynx, the apparatus generates positive end-expiratory pressure in the lower respiratory tract depending on the flow and whether the person breathes with his mouth open or closed [9]. This effect works similarly to continuous positive airway pressure, preventing the alveoli from collapsing on exhalation. The conducted research suggests an increase of approx. 0.69 cm H_2O for every 10 L/min of flow in the case of ventilation with the mouth closed and approx. 0.35 cm H_2O with the mouth open [9].

Many high-flow oxygen therapy devices have built-in heating and humidifying systems. Providing adequately humidified air at an appropriate temperature significantly improves the patient's ventilation comfort [10]. A properly heated and moistened breathing mixture prevents drying of the respiratory epithelium and improves mucociliary cleansing [11, 12].

When using high-flow oxygen therapy, the supplied breathing mixture does not mix with the atmospheric air in the respiratory tract. Thus, the concentration of the oxygen supplied in the respiratory tract is very close to the FiO_2 value set on the device, unlike conventional passive oxygen therapy [13, 14].

HFNOT: its application in patients with COVID-19-related pneumonia and respiratory failure

The above-described mechanisms of action of high-flow intranasal oxygen therapy cause adequate oxygenation of the respiratory mixture, reduction of respiratory frequency, reduction of respiratory effort, an increase of PEEP and end-tidal volume of the lungs, and adequate hydration of the respiratory mixture. High-flow oxygen therapy has been used in treating hypoxemia in severely spontaneously breathing patients who do not require the use of more advanced mechanical ventilation techniques. [3, 15, 16]. Accordingly, HFNOT may play an important role in the treatment of acute hypoxemic respiratory failure in the course of Sars-CoV-2 infection.

Xiao-bao Teng's 2020 study on a group of 22 patients confirmed the validity of the early use of high-flow oxygen therapy in patients with respiratory failure in the course of COVID-19 compared to conventional passive oxygen therapy. Patients who received HFNOT had better HR, RR, and PaO2 / FiO2 after six hours of the experiment and better PaO_2/FiO_2 after 24 and 72 hours. The study also showed reduced hospitalization time when using high-flow oxygen therapy [17].

A large Chavarria study from 2021 also confirms the effectiveness of HFNOT. The use of a high-flow oxygen cannula led to an improvement in respiratory parameters in many Covid19 patients. The use of HFNOT successfully prevented endotracheal intubation in 71.4% of patients (270 out of 378) with hypoxemic respiratory failure. Patients who successfully received HFNOT also had a much shorter stay in the hospital and less frequently required admission to the ICU [18].

Gorshengorn published interesting results in his work. He proved that using a high-flow nasal cannula combined with early mechanical ventilation resulted in fewer deaths and greater availability of ventilators. At the national level, this strategy resulted in 10,000–40,000 fewer deaths than if a high-flow nasal cannula were unavailable. In addition, with the country's moderate ventilator performance (30,000–45,000 ventilators), this strategy led to up to 25 (11.8%) fewer days with no ventilators available. In a 250-bed hospital with 100 mechanical ventilators, the availability of 13, 20, or 33 high-flow nasal cannulas prevented 81, 102, and 130 deaths, respectively [19, 20].

In adult patients with moderate and severe COVID-19 treated with HFNC, the SOFA scale and ROX index may help identify patients with a higher probability of intubation (18). ROX > 3 at 2.6 and 12 hours after initiating high-flow oxygen therapy is sensitive to the identification of HFNC success [21] and has good discriminatory power in predicting HFNC failure in patients with COVID-19 respiratory failure [22].

Duan's 2020 observational study compared HFNC and non-invasive ventilation as first-line treatment in critically ill patients with COVID-19. Duration of NIV and HFNOT, intubation rate, and mortality were similar in both groups [23]. Compared to both methods of oxygen therapy, high-flow oxygen therapy is distinguished by greater comfort of use for the patient [24]. The HFNOT interface, compared to NIV, causes less skin damage, allowing the patient to speak, cough and eat freely [25]. The operation of the high-flow oxygen therapy device is much easier and more intuitive than the NIV devices, making the medical staff more inclined to use HFNOT in patients with respiratory failure [26]. However, both ventilation methods require close monitoring of patients to avoid delaying the need for intubation. Delayed intubation significantly increases mortality in both HFNC and NIV patients [27, 28].

Simiola et al. showed that high-flow oxygen therapy is safe and effective for ventilation in patients with severe respiratory failure in the course of COVID-19 and plays a positive role in related complications, such as pneumomediastinum and pneumothorax. [29]. Among severe forms of ARDS, the cure rate for pneumonia pneumothorax was 70% with HFNC.

Research suggests that a Prone Position (PP) may increase PaO_2/FiO_2 and reduce mortality in moderate to severe acute respiratory syndrome. The 2020 Xu Q study demonstrated that early use of PP in combination with HFNOT in patients with severe COVID-19 may reduce the need for intubation and mechanical ventilation [30]. The definition of acute respiratory distress syndrome (ARDS) has been evolving in recent years. The latest version — the Berlin 2012 criteria has been widely adopted and used worldwide. Since that day — the ARDS definition was expanded and included patients with an initial PaO2/FiO2 lower than 300 mm Hg and receiving either invasive or non-invasive ventilation with a tight-fitting mask and generating PEEP (or Continuous Positive Airway Pressure — CPAP) ≥ 5 cm H_2O. The role of HFNO in treating COVID-19 pneumonia and respiratory failure has been unprecedented though more and more researchers and experts suggest another expansion of the ARDS criteria to include patients on HFNOT with at least 30 L/min who fulfil other criteria for the Berlin definition. The new version would make the diagnosis of ARDS more widely applicable, focusing on patients with sufficient clinical lung injury to require high levels of oxygen support, independent of the necessity for mechanical ventilation [31]. Raoof et al. advocate oxygen supplementation with HFNC for COVID-19 patients with mild to moderate respiratory distress, increased work of breathing, $PaO_2/FiO_2 > 150$ but < 300, or $SpO_2 < 90–94\%$ on non-rebreather. They propose immediate invasive mechanical ventilation in patients with severe respiratory distress, $PaO_2/FiO_2 < 150$, or $SpO_2/FiO_2 < 196$ [32]. The greatest danger when using HFNOT, especially with patients with COVID-19, is to fail to monitor closely enough, leading to an unanticipated need for intubation. Indicators of impending failure include increasing tachypnoea and tachycardia, failure to adequately support oxygenation despite a high flow rate and FiO_2, a climbing $PaCO_2$ in a struggling patient, development of dyssynchronous breathing, alteration in mental status, and haemodynamic instability [32].

Clinical use of HFNOT in managing exacerbations of COPD

Chronic Obstructive Pulmonary Disease (COPD) exacerbations are a common cause of hospitalization worldwide. Depending on the severity, they may be accompanied by acute respiratory failure. The ERS/ATS and GOLD-COPD guidelines recommend the application of non-invasive ventilation (NIV) for patients with acute respiratory failure, hypercapnia, and acidosis (pH 7.35). A significant number (up to 64%) of NIV failure, mainly due to mask intolerance and desynchronization with the ventilator is the reason for searching for alternative ways to support patients with COPD exacerbations. There is still a limited number of clinical trials regarding the use of high-flow oxygen therapy in treating such patients. Pisani et al. presented a systematic review of the literature on HFNOT and its adoption in exacerbated COPD patients. They showed a number of trials where HFNOT proved to be non-inferior in regard to NIV in improving gas exchange, PaCO2 reduction, and alleviating the work of breathing while keeping all the benefits of patient comfort. Further studies are necessary, yet HFNOT might prove to be a good alternative to NIV in patients with COPD exacerbation with mild-to-moderate respiratory acidosis (i.e., $7.25 < pH < 7.35$) [33, 34].

HFNOT: enhancing patient care through its application in the intensive care unit

Incidents of respiratory distress after extubating in intensive care are quite common, and according to various sources, their frequency ranges from 6 up to 47% [35]. Rittayamai's research showed better HFNOT application effectiveness than conservative oxygen therapy, especially in reducing the breathing rate, dyspnoea and heart rate [36]. Maggiore and Hernandez brought similar results in their studies [37, 38]. However, both studies relate to patients with a low risk of reintubation. In the case of patients with a higher risk, it seems advisable to consider the implementation of the NIV and use HFNOT only as a supporting method when NIV is not in use.

Employing HFNOT to optimize patient care during bronchoscopy

There are reports of a beneficial effect of using HFNOT during bronchoscopy, especially in patients with respiratory dysfunction. Application flow of 50–60 L/min and FiO_2 0.6–1.0 allows the procedure to be carried out with good tolerance by the patient and only slight fluctuations in arterial blood saturation during the procedure [39, 40].

HFNOT: its applications in cardiology and cardiothoracic surgery

It appears that a high-flow ventilation oxygen therapy by improving oxygenation at

a relatively low increase in chest pressure may benefit patients with acute cardiogenic pulmonary oedema. Unfortunately, there are few reports confirming such an assumption and they have rather the nature of the case reports, hence it is rather here a suggested consideration of the options and not an actual recommendation for the use of HFNOT [41]. Studies by Park and Frat support a particular recommendation for the application of high-flow oxygen therapy after cardiac and thoracic surgery. They found that the use of HFNOT significantly reduces the number of desaturation episodes, reduces the need to implement NIV and also the rate of necessary reintubation while maintaining no differences in haemodynamic parameters between the patients' groups [9, 42]. Corley et al. presented an increase in EELV (End Expiratory Lung Volume) of 25.6%, TV (tidal volume) by 10.5% and mean airway pressure by 3 cm H_2O in comparison to the group of conventional oxygen therapy [43].

HFNOT: its spplications in neonatology and paediatrics

Non-invasive ventilation and CPAP respiration support are common practices to treat respiratory failure in preterm infants. However, despite the passage of time and significant technological progress, a significant percentage of these children still suffer from long-term consequences, including the need for postnatal ventilation.

Studies conducted in the neonate population and fairly recently among infants have shown that HFNOT is an effective therapy in this population. Mayfield et al. showed a significant reduction in paediatric intensive care unit (PICU) admissions in infants with bronchiolitis receiving HFNOT. They were four times less likely to be admitted to PICU in comparison to the standard treatment group [44]. In a retrospective analysis Schibler et al. showed that since the introduction of HFNOT in the paediatric intensive care unit, the need for intubation and mechanical ventilation in infants with viral bronchiolitis decreased significantly over the 5 years, from 37% to 7% [45]. Similar data were presented in a study by McKiernan et al where the reduction rate was observed from 23% to 9% [46].

Conclusions

High-flow oxygen therapy plays an important role in the management of acute hypoxemic respiratory failure associated with Sars-Cov-2 infection. Its superiority over conventional oxygen therapy is well documented as it improves respiratory parameters, reduces mortality, prevents intubation and shortens hospitalization in some patients with acute respiratory failure. It is a safe, non-invasive method, well-tolerated by patients and willingly chosen by medical personnel.

HFNOT devices can be effectively used in spontaneously breathing patients with severe respiratory failure during COVID-19, whose condition does not require the use of advanced mechanical ventilation techniques with high PEEP. Indications for HFNOT in the Setting of Acute Respiratory Failure are $PaO_2 < 65$ mmHg or saturation < 90% on supplemental oxygen, respiratory rate > 25, mild ARDS defined by $PaO_2/FiO_2 < 300$ but > 200.

Early introduction of HFNOT along with the prone position can significantly improve gas exchange and patient outcomes. It also plays a positive role in COVID-19-related complications such as pneumomediastinum and pneumothorax.

It should be emphasized that high-flow oxygen therapy is not a method that replaces mechanical ventilation, including NIV. Persistent high respiratory rate and/or respiratory failure are associated with an increased risk of HFNOT failure. Therefore, it is very important to carefully monitor patients with HFNOT to avoid prolonged treatment and not delay intubation. Moreover, this treatment method is most well tolerated by patients and does not require specialized and long-term personnel training.

HFNOT has proved to be a safe, non-invasive method, essentially risk-free. It has a variety of appliances in modern medicine. Not only in pulmonology/intensive care unit but also in other fields of medicine.

Article information

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