



REVIEW

High-Flow Nasal Oxygenation and Its Applicability in COVID Patients

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Abstract

High-flow nasal oxygenation (HFNO) is a type of oxygen therapy that provides humidified and heated oxygen through a nasal cannula at much higher flow rates than standard oxygen therapy, while also allowing control over the fraction of inspired oxygen (FIO₂). Compared to standard oxygen therapy, it is much more comfortable for the patient and seems to alleviate most of the problems associated with standard oxygen therapy, such as dry nose, dry throat and nasal pain. It also provides a variety of benefits that can reduce the incidence of escalating treatment and initiating mechanical ventilation in COVID patients with acute hypoxemic respiratory failure (AHRF). This article provides an overview of HFNO and its current applications in COVID patients during the pandemic.

Keywords High-flow nasal oxygenation · COVID · Anaesthesia · Intensive care · Oxygen therapy · Pre-oxygenation · Respiratory failure

Introduction

Supplemental oxygen therapy has a vital role in treating critically ill patients, where hospitals have a wide array of modalities to choose from. It is routinely used to maintain adequate oxygen saturation as well as alveolar ventilation. During normal breathing cycles, air is passed through the nose, pharynx, larynx and trachea, where there is significant humidification and heating of the air [1]. In the upper airways, the air is fully saturated with water; however, when given supplemental oxygen, this biological phenomenon ceases, particularly at low flow. This is the primary cause for the symptoms experienced by patients, including dry nose, dry throat and nasal pain, while reducing nasal mucociliary clearance, which results from inhalation of medical gases that were not humidified and heated [2, 3]. Most oxygen supplement devices are limited to no more than 15L/min, while the required flow rates for patients with respiratory failure

can be up to 10 times this rate [4]. The large difference between patient inspiratory flow and delivered flow results in an inconsistent inspiratory fraction of oxygen (FIO₂).

High-flow nasal oxygenation (HFNO) has become increasingly common in many acute care settings, as it minimizes discomfort for the patient associated with low-flow oxygen supplementation, while additionally decreasing the dead space and increasing alveolar ventilation [5]. However, HFNO cannot actively change tidal volume as it is unable to provide an inspiratory push nor an expiratory pull due to its open circuit [6]. HFNO is a supplemental oxygen device that is comprised of an air/oxygen blender, humidifier, nasal cannula and heated tube that can provide a gas flow of up to 70 L/min [7]. HFNO is an innovative and more efficient method of delivering supplemental oxygen, which is deemed to be more ideal for patients with respiratory failure as demonstrated by its use during the COVID pandemic [8]. This article will provide an overview of HFNO as well as the role it has played during the COVID pandemic.

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High-Flow Nasal Oxygenation

HFNO is an alternative modality to standard oxygen therapy, which is the result of a multi-decade process to provide a system that could deliver both heated and humidified oxygen

at high flows. Starting flow rates of 1 L/kg/min with a maximum of 2 L/kg/min are recommended [9]. However, in clinical practice, starting flow rates of 30–40 L/min are routinely used, while up to 70 L/min can be delivered. In infants, the flow is typically determined by weight, rarely exceeding 8 L/min. It is a circuit made up of an air/oxygen blender connected to a nasal cannula via a humidifier and heated tube, which allows for the control of FIO₂ (0.2 to 1.0) independently of the flow rate [10]. As previously mentioned, due to the humidification and heating of oxygen, patients are relieved of the common symptoms attributed to standard oxygen therapy, such as dry throat and dry mouth.

Mechanisms

HFNO has a positive role in increasing ventilatory efficiency by a variety of mechanisms. It can constantly flush out carbon dioxide from the nasopharynx, which eliminates the dead space in proportion to the flushed-out volume, increasing FIO₂ [11, 12]. This further allows for a greater proportion of the minute ventilation to participate in gas exchange [13]. Additionally, many studies have shown the effects of HFNO on positive end-expiratory pressure (PEEP) [14–17], which has the potential for application in ICU and perioperative settings as it prevents the cyclical opening and collapsing of alveoli [18]. The airway pressures are dependent on the flow rate, upper airway anatomy, whether breathing through the mouth or nose, and the cannula to nostril size ratio [16, 17, 19]. However, air leakage through the nose and mouth contributes to the variable pressure levels obtained (mean values ranging between 2.7 and 7.4 cm H₂O) [20]. Furthermore, the PEEP effect of HFNO increases tidal volume and end-expiratory lung volume and decreases the respiratory rate and left ventricular afterload, while preserving minute ventilation [21–23]. These alterations in the breathing pattern are a result of recruitment of previously collapsed alveoli or further distention of already ventilated alveoli, similar to the effects achieved with continuous positive airway pressure (CPAP) [24, 25]. This has shown to be beneficial in patients suffering from acute cardiogenic pulmonary oedema and acute heart failure [26, 27].

Indications and Contraindications

HFNO is indicated in cases of acute hypoxemic respiratory failure (AHRF) of any cause, post-extubation respiratory failure, pulmonary oedema and apnoeic oxygenation and in other respiratory diseases (pneumonia, exacerbation of COPD, bronchitis and bronchiectasis, etc.), where the patients tend to have increased secretions and difficulty expelling them [9]. HFNO is contraindicated in cases of suspected pneumothorax, facial nasal and oropharyngeal and oesophageal trauma. Endotracheal intubation would be

preferred in unconscious patients and patients with respiratory failure refractive to HFNO or other non-invasive ventilatory modalities [5].

Effects in Acute Hypoxemic Respiratory Failure

AHRF can cause respiratory muscle fatigue as well as the loss of airway cells that play a role in the physiological humidification of air, resulting in mucus plugs [28]. HFNO is, therefore, a vital modality to ensure the proper humidification and heating of air to 37 °C, which preserves adequate mucosal function in gas exchange, limiting the metabolic cost of breathing, and preserves the mucosal role in host defences [29]. Additionally, the consistency and volume of respiratory secretions are preserved, as well as the potential to maximize mucociliary clearance. All of these mechanisms contribute to a reduction in the metabolic cost of breathing, which is beneficial especially in patients with AHRF [30, 31]. Furthermore, patients with AHRF typically have larger inspiratory flow rates exceeding those of standard oxygen therapy, which allows entrained room air to dilute the supplemental oxygen, further reducing FIO₂ [32]. However, HFNO provides much higher flow rates, which exceeds these patients' inspiratory flow rate, thereby allowing for less dilution of oxygen and delivery of a more desirable FIO₂ [33]. HFNO with open mouth breathing tends to dilute the supplemental oxygen reducing the desired FIO₂, in contrast to closed mouth nasal breathing with HFNO which raises the FIO₂ [34]. Furthermore, studies comparing patients with AHRF oxygenated via a facemask compared to HFNO all demonstrate that HFNO provides better oxygenation, comfort and tolerance; however, oxygenation is only better with HFNO during closed mouth breathing [35–37].

Induction During Anaesthesia

HFNO also has a variety of roles in the anaesthetic management of patients in the operating theatre during induction and maintenance of anaesthesia. Specifically, patients with anticipated difficult airways, such as morbidly obese patients (BMI > 35 kg/m²) and patients with underlying airway diseases, are routinely pre-oxygenated using HFNO, as the common technique for intubation in these patients is awake fibre-optic intubation, which exposes them to a higher risk of hypoxemia [38]. Normal facemask ventilation in these patients may only provide a safe apnoea period of 1–3 min following pre-oxygenation compared to 7–10 min in normal healthy adults since there is a decrease in functional residual capacity and an increased oxygen consumption due to obesity-related physiological changes. HFNO has been shown to improve oxygenation, patient tolerance and safety, as it results in a larger concentration of oxygen available to maintain saturation during apnoeic episodes during long and

difficult intubations when compared to facemask ventilation in morbidly obese patients [39, 40]. Additionally, in normal cases post-induction, the face mask is removed to attempt tracheal intubation. During this time, there is no oxygen supplied, posing a risk of hypoxemia in case of prolonged intubation [41]. HFNO can prove to be advantageous in these situations, as the nasal cannula does not need to be removed during the insertion of airway devices as well as attempts at laryngoscopy, thus allowing for better oxygenation during these techniques. However, it has been noted that although HFNO provides better oxygenation during the induction process—consistently achieving higher oxygen saturation—this effect ceases after induction, when bag-mask ventilation with a face mask supersedes it in maintaining oxygen saturation post-induction [42], highlighting the superiority of HFNO during the induction phase of anaesthesia.

Application in COVID Patients

During the COVID pandemic, the SARS-COV-2 virus has spread rapidly throughout the globe, resulting in millions of deaths. The majority of hospitalized COVID patients present with AHRF, with a minority of them requiring treatment in the ICU [43]. COVID patients requiring invasive mechanical ventilation have a mortality rate of about 40%, which added to the limited availability of ICU beds, requires physicians to avoid intubation, when possible. Due to this, the requirements of non-invasive respiratory modalities, such as HFNO, are continuously being adopted to treat patients with AHRF secondary to COVID, where their use has been successful in avoiding escalation of treatment and/or intubation [44–47].

Delayed Tracheal Intubation and Mechanical Ventilation

HFNO has shown the possibility of reducing the relative risk of requiring invasive ventilation and escalation of oxygen therapy in patients with AHRF [48]. Intubation of patients by anaesthesiologists is a vital component of managing COVID-19 patients, many of whom experience AHRF. Often there is limited time to secure the airways of patients, hence, the use of HFNO may provide a few additional minutes to aid anaesthesiologists in prolonged periods of intubation. A prospective randomized controlled trial was conducted for the use of HFNO-assisted fibre-optic tracheal intubation in critically ill patients which showed a decrease in the time needed to intubate as compared to the standard mask oxygenation group [49]. The HFNO group showed a smaller decrease in SpO_2 . Furthermore, a meta-analysis that included 31 studies with 5136 participants has concluded that HFNO may reduce the drop in oxygen saturation while

treating COVID patients as compared to standard oxygen therapy [50]. Additionally, an observational study in Italy where there is a lack of ICU beds has shown that the use of non-invasive respiratory support such as HFNO is a practical way to decrease unfavourable outcomes outside the ICU setting in patients with COVID [51]. An additional study in Paris, where a total of 138 patients with COVID-related acute respiratory failure were evaluated to compare HFNO to standard oxygen therapy [46], found that only 51% of those on HFNO required invasive mechanical intubation, compared to 74% of those on standard oxygen therapy. Furthermore, a South African study included 293 patients with AHRF secondary to COVID [52]. HFNO was delivered at a rate of 50–60 L/min with FiO_2 0.8–1.0 aiming to maintain $SpO_2 \geq 92\%$. The rate of successful outcomes was found to be 47%. Higher SpO_2 , lower heart rate, lower respiratory rate and lower oxygen requirements at the admission predicted a successful outcome. The ratio of SpO_2/FiO_2 to respiratory rate measured 6 h post-HFNO initiation > 3.7 was found to be 80% predictive of success. Other studies in non-COVID-related AHRF have also concluded that there is reduced requirement for intubation using HFNO [53–55]. These studies show that there is a positive correlation between incorporating HFNO in COVID patients to prevent escalation of disease and further intervention. However, due to the limited data available, the use of HFNO in COVID patients cannot be promoted nor refuted. Its use is limited to guidelines from international and national organizations, expert opinions and institutional culture.

Aerosolization and Spread of Virus Particles

The aerosolization of infectious particles during the induction of HFNO must be considered for the safety of doctors and nurses [48]. The use of HFNO in COVID patients has been limited due to concerns of increased aerosolization; however, numerous studies suggest it is safe to use, with additional benefit from appropriate personal protective equipment (PPE) worn by the medical workers and face masks worn by the patients. Aerosols are defined as respiratory particles smaller than $5 \mu m$ [56]. Smoke laser experiments have shown that the use of 60L/min HFNO corresponds to a similar spread of aerosolized infectious particles as compared to standard oxygen therapies [57]. Dispersion of exhaled smoke (aerosol of solid particles $< 1 \mu m$) was visualized in a simulation on a manikin model. It revealed that utilizing HFNO at 60L/min resulted in dispersion comparable to regular oxygen masks at 15L/min and resulted in lower dispersion compared to other methods such as non-rebreathing masks and Venturi masks. Therefore, the airborne transmission of COVID does not appear to be greater in HFNO compared to a regular oxygen mask [57–59]. Surgical masks have also been shown to be

effective during normal breathing through a computational fluid dynamic simulation study [60, 61]. In a human patient simulator model, bursts of oxygen flow mimicking coughing bouts suggest that the aerosolization of infectious particles travels a distance on average of no more than 65 cm, which can be further reduced to around 30 cm with adequate use of a surgical mask on top of the HFNO cannula during coughing [62]. Additionally, the use of surgical masks seems to improve oxygenation when worn on top of HFNO. The use of a surgical mask resulted in an increase in PaO₂ and SaO₂ [63].

Some theories support HFNO in decreasing aerosolized particles created due to oxygen therapy. One explanation is that aerosol particles are formed via shear stress during turbulent flow and vocal cord vibration [64, 65]. Coughing produces a flow rate of about 400L/min while HFNO uses 60L/min which might not be sufficient to create aerosols [66, 67]. Another theory involves the opening of closed bronchioles which in turn releases particles from the walls of the bronchioles. In case the latter theory is correct, the use of HFNO therapy can be beneficial as it creates a PEEP, which hinders the closure of smaller bronchioles [68]. In **conclusion**, even though the aerosolization of infectious particles is possible, it appears to be not as severe as previously thought. The use of a surgical mask on top of the HFNO cannula in addition to the use of PPE by hospital staff should minimize the spread of COVID aerosols.

Conclusion

In summary, HFNO is a type of oxygen supplemental therapy that can deliver oxygen at high flow rates up to 70L/min, while simultaneously being able to provide a FIO₂ between 0.21 and 1.0. It has numerous physiological effects such as pharyngeal dead space washout, a reduction in the work of breathing, a PEEP effect, constant FIO₂ release and increased mucociliary clearance, all of which are useful in treating patients presenting with AHRF secondary to COVID. The use of HFNO in COVID patients has reduced the need to intubate or escalate treatment in approximately 50% of cases and with no increased risk of aerosol transmission compared to standard facemasks, HFNO is a viable candidate to manage COVID patients and help aid the ICU bed shortage in the pandemic.

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Code Availability Not applicable.

Declarations

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Conflict of Interest The authors declare no competing interests.

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