High Flow Nasal Cannula: Current Status in Covid-19

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ARTICLE INFO

Abstract

The Coronavirus disease (COVID-19) has been declared as a global pandemic and has posed major challenge upon the healthcare system. It has a wide range of clinical presentation, ranging from a mild flu-like symptoms to moderate respiratory illness progressing to severe or fatal disease. The seriously ill COVID-19 patients present with acute respiratory failure. The oxygen therapy is the most useful and the mainstay of treatment in COVID-19. The conventional modes of oxygen therapy for respiratory support such as simple and high flow face masks, nasal prongs, venturi masks, non-invasive ventilation masks (NIV) and even invasive ventilation using endotracheal tube are used in COVID-19 patients. The conventional modes provide low flows of oxygen and difficult titration. Use of high flow nasal cannula (HFNC) in COVID-19 associated respiratory failure is a relatively newer mode of oxygen therapy. It delivers warmed and humidified oxygen via nasal cannula at higher flows, which provides better titration of FiO₂ along with better tolerance and compliance of the patient. HFNC device has many physiological and clinical benefits in acute hypoxemic respiratory failure. Its usefulness has been studied in many clinical scenarios such as in critical care and operation theatres as well as in palliative care. This brief review summarizes the usefulness and clinical benefits of HFNC along with its risks for the treatment of hypoxemic respiratory failure in moderate to severely ill COVID-19 cases.
INTRODUCTION:
Coronavirus disease (COVID-19) is an infection with fatal complications, which surfaced in China and now has been declared as global pandemic. It is caused by the novel coronavirus (SARS-CoV-2)\(^1\). It has spread globally due to its highly contagious nature, while many patients develop mild flu-like symptoms, some develop pneumonia like features needing hospitalization and some need supportive respiratory management in critical care units. The main symptoms observed are fever, cough, breathlessness, muscle aches, tiredness and radiological infiltrates or pneumonia\(^2,3\). As COVID-19 has wide spectrum of clinical severity; many patients develop profound arterial hypoxemia yet no conventional signs of respiratory distress or breathlessness\(^4,5\). This scenario is referred as “Silent Hypoxemia”. The pathophysiology of such hypoxemia (figure1) is still unclear but various causes include loss of lung perfusion regulation, intravascular thrombi formation, intrapulmonary shunting and impaired diffusion capacity along with leftward shift of oxyhemoglobin curve, leading to rapid clinical deterioration and need of artificial respiratory support\(^6\). Thus, the major healthcare challenge associated with COVID-19 is the safe delivery of respiratory support via selection of appropriate devices for administration of oxygen.

![Figure 1. Pathophysiology of Happy Hypoxemia in COVID-19\(^6\) (Reproduced with permission)](image)

Initially, approach for COVID-19 treatment revolved around invasive mechanical ventilation and lung protection measures\(^7\). Later, other strategies emerged for use in patients with respiratory failure who do not need mechanical ventilation. Administration of oxygen is an essential measure to maintain adequate tissue oxygenation in patients with acute hypoxic respiratory failure associated with coronavirus disease. Various techniques are available for delivery of oxygen such as conventional oxygen therapy devices i.e low, intermediate and high flow devices and non-invasive and invasive ventilation. Nowadays, High Flow Oxygen via nasal cannula, combined with heated humidification system has been increasingly used method of oxygen therapy, especially in patients with acute hypoxic respiratory failure consequent to coronavirus disease.
RESEARCH METHODOLOGY
This review on the HFNC use in coronavirus affected patients was carried out using databases from PubMed, Web of science, Google Scholar etc. The terms such as High flow nasal cannula, acute hypoxemic respiratory failure, COVID-19, Coronavirus disease were used for search. The research was restricted to articles in English language and done till March 2021 and studies which did not include HFNC were not taken into account.

DEVICE DESCRIPTION
HFNC was earlier used in pediatric population for respiratory distress management. Now, it has been increasingly used in adult patients as an alternative mode of supplementation of oxygen in different clinical scenarios. HFNC is a device used to deliver oxygen at high flows of up to 50-60l/min along with warmth and humidification by the use of an interface made up of silicone cannula that fits without obstructing the nose. It is an open-circuit framework comprising of a steam generator, a humidifier and single limb non-condensing circuit. This circuit can be attached with a silicone cannula of various sizes to fit patient’s nostrils. It can deliver up to 60l/min of heated, humidified oxygen at 37 degree Celsius with 100 percent of relative humidity via nasal cannula (figure 2). It overcomes the limitations of flow of gas in low and intermediate flow oxygen devices. The flow independent titration of FiO2 can be achieved via oxygen mixer, attached to the circuit, ranging from 0.21 to 1.0.

CLINICAL EFFECTS OF HFNC
The major clinical benefit of HFNC is the flow-dependent delivery of oxygen. Increase in flow leads to augmentation in FiO2. Maximum benefit can be achieved by matching flow to patient’s inspiratory demand. It can deliver set fraction of FiO2 better than other oxygen therapy devices by reduction of air entrainment and avoiding air dilution. HFNC reduces the anatomical dead space by removal of carbon-dioxide out of the nasopharyngeal space or upper airway. Consequently, higher fraction of minute ventilation is delivered to the alveoli where it participates in gaseous exchange. Subsequently, work of breathing is improved and respiratory rate is reduced and respiratory efforts become more efficient. HFNC also provides a low level positive pressure, which can increase lung volumes and improve gas exchange.
Major physiologic mechanisms of HFNC useful in patients of coronavirus disease are decreased respiratory rate, low positive end expiratory pressure (PEEP), raised tidal volume, increased end expiratory lung volumes, reduced dead space, washout of carbon dioxide and better comfort with decreased work of breathing.

Corley et al demonstrated higher end expiratory volumes with the use of HFNC than with other devices providing low flows. The delivery of conditioned gas by HFNC is associated with increased conductance and improved lung compliance which further enhances mucociliary function and facilitates clearance of secretions, reduced atelectasis along with improved ventilation/perfusion ratio and oxygenation. Parke et al demonstrated that HFNC generates positive pressure in nasopharynx, more in expiratory phase thus providing low level PEEP. Thus, HFNC was considered in the frontline management for patients with hypoxemic respiratory failure associated with COVID-19 infection.

The FLORALI Trial demonstrated that HFNC reduced the risk of mechanical ventilation in patients with acute respiratory failure having PaO2/FiO2 less than 200 and also decreased the death rate in patients accepting HFNC therapy. In a study conducted by Arnav Aggarwal et al on the application of HFNC in COVID-19 patients demonstrated that when applied to respiratory failure patients of COVID-19, it substantially reduced risk of progression to NIV and invasive ventilation.

An observational study conducted by G.L Calligaro et al for utilization of HFNC for severe cases of coronavirus disease, primarily concluded that HFNC is most feasible in a resource-constrained setting and patients can be easily weaned off from it, avoiding invasive ventilation. Out of 293 patients enrolled in the study, 137 patients were successfully weaned off from HFNC. Another study was done by Vianello A et al, to assess the outcome and safety of oxygen therapy by HFNC in 28 patients with severe COVID-19 infection, unresponsive to conventional oxygen therapy. 19 patients had a positive response and 9 patients required escalation to NIV. The study suggested that HFNC is a safe treatment for patients with less severe SARS-CoV-2 infection. Another retrospective study was done by Hu et al for checking utilization of HFNC in hypoxemic coronavirus disease patients. Out of 105 patients, 65 patients demonstrated better oxygenation and were weaned off early from HFNC. The study concluded that HFNC is a reliable method of respiratory support in COVID-19 and predicted a good outcome.

A multi-center, retrospective cohort study was done by Xia et al on use of HFNC in cases of coronavirus affected acute hypoxic respiratory failure, in which 43 adult patients with confirmed coronavirus disease 2019 were enrolled. It was concluded that HFNC therapy was effective for treatment of mild to moderate cases of respiratory failure of coronavirus disease and its failure was associated with poor prognosis.

The most important question is whether HFNC is more efficient than other non-invasive respiratory therapies of oxygenation. Multiple meta-analysis and researches which compared conventional oxygen therapies, NIV and HFNC have been done. Various studies have been conducted to compare HFNC with NIV and HFNC has been proven to be more tolerable and better suited to the patients. It improved oxygenation better than another conventional oxygen flow devices. Conventional oxygen therapy includes administration of oxygen using nasal prongs or face mask at low flows up to 15 litres/min only and without humidification and heat which may cause discomfort to the patient as the flow is increased. While NIV, which can be coupled with conventional oxygen therapies, is an advanced method for improving ventilation, it still can cause discomfort due to high pressures generated in the airways, difficulty in breathing synchronization, claustrophobia and mask related effects such as skin soreness. HFNC is a flow-generator and has its beneficial effects of reliable delivery of targeted FiO2 via high flow while NIV in contrast is a pressure-generator and its pressure transmission provides beneficial effects.
Evidence seems to suggest that HFNC showed reduced rate of mechanical ventilation and intubation compared to conventional oxygen therapies when used with caution\textsuperscript{30}. Frat et al\textsuperscript{31} compared HFNC with oxygen therapy via NRB mask and with NIV mask along with pressure support for achieving tidal volume of 8-10 ml/kg. It was observed that there was a significant reduction in rate of intubation in HFNC group in patients having PaO2/FiO2 less than 200. It was concluded that HFNC offers wide range of advantages over standard oxygen devices and NIV and should be considered as first line consideration in mild and moderate hypoxemic respiratory failure.

A study from France compared HNC to conventional oxygen therapy in a group of 379 coronavirus affected patients. They concluded that HFNC significantly reduced the need of mechanical ventilation and it was safe and effective\textsuperscript{32}.

In another prospective randomized study, researchers compared HFNC to oxygen therapy by face mask at approximately similar FiO2 and concluded that HFNC improved oxygenation, decreased respiratory rate and minute ventilation\textsuperscript{11}. According to Surviving Sepsis Guidelines on treatment of critically ill COVID-19 patients: HFNC over NIV is recommended in coronavirus affected adults and in patients with acute hypoxemic failure\textsuperscript{7}.

**ROLE OF HFNC IN OTHER CONDITIONS**

1) HFNC can be used in pre-oxygenation/apneic oxygenation in a difficult airway manage-ment. As patients tolerate HFNC better than tight face masks and it delivers high flows up to 60l/min which can denitrogenate the lungs faster than standard flow rates of 10-15 l/min\textsuperscript{33}. Also it can be kept in situ during laryngoscopy enabling apneic oxygenation. HFNC can re-duce risk of desaturation in obese patients during induction of anaesthesia\textsuperscript{34}. It is used as a part of THRIVE (Transnasal Humidified Rapid Insufflation and Ventilatory Exchange) during laryngeal surgeries. Booth et al\textsuperscript{35} have advised the use of HFNC for anaesthetized patients with history of previous difficult intubation who tolerated micro laryngeal surgery with minimal desaturation.

2) HFNC is easier to apply and optimize pre-oxygenation before any emergency endotracheal intubation in patients with severe respiratory depression; as shown in a study which concluded HFNC as effective as the standard face mask or bag-valve mask for pre-oxygenation with no life-threatening desaturation\textsuperscript{36,37}.

3) HFNC can also be applied in post-surgical patients for improving oxygenation after any major surgery.

4) HFNC following extubation can be utilized for optimizing oxygenation which reduces the risk of re-intubation in ICU settings. In a meta-analysis, HFNC was shown to reduce the rate of re-intubation compared to the use of conventional oxygen therapies and NIV and did not affect length of ICU stay\textsuperscript{22}.

5) Mortality is usually higher among immunosuppressed patients who need artificial respiratory support\textsuperscript{38}. HFNC has been found to be more beneficial than other conventional oxygen therapy or NIV among such patients\textsuperscript{39}.

6) Use of HFNC in end stage COPD, when NIV is not feasible during exacerbations, improved the patient tolerance and compliance\textsuperscript{40}. HFNC can be further used for domiciliary treatment of COPD and respiratory failure which reduces the risk of mortality.

7) In Obstructive Sleep Apnoea (OSA), HFNC is now explored as an alternative to CPAP for better comfort. Also, it can be used as palliative care measure in breathlessness as it provides better comfort level compared to face masks\textsuperscript{41}. It is better tolerated by patients with terminal critical illness with respiratory failure\textsuperscript{42}.

8) HFNC can also be applied during bronchoscopy and has a promising role in management of cystic fibrosis and bronchiectasis in which mucus hypersecretion and reduced clearance is the major problem\textsuperscript{43}.
9) HFNC has been shown to be effective in management of acute cardiogenic pulmonary oedema by increasing oxygenation while decreasing cardiac after load by generating a low positive intra-thoracic pressure.

ADVANTAGES OF HFNC
Therapeutic effect- In COVID-19 patients, oxygen therapy is the best and first line basic treatment. Application of HFNC reduced the intubation rates and need of invasive ventilation. As patients with coronavirus disease have bad prognosis after invasive ventilation and have associated complications, HFNC offers best alternative management. HFNC provides a reliable triad of humidity, high FiO2 and improved patient tolerance.

It reduces the workload of healthcare workers. HFNC is better tolerated by the patients, thus, showing better compliance and safety when long term oxygen treatment is needed; as HFNC is only applied to nostrils, patients continue to eat and speak normally. Nursing Care such as oral suctioning can be done easily and medication can be administered without discontinuation of oxygen therapy.

Prevention of nosocomial infection as HFNC has low range of diffusion of exhaled gases which reduces the spread of virus, when cannula is worn adequately. Non-standard ICU’S do not have negative pressure area and have normal exhaust system, thus leading to higher load of the virus. HFNC is suitable for such ICU’S and surgical mask can be worn along with it to reduce aerosol transmission. As COVID-19 spreads mainly through respiratory droplets, a significant concern arises for use of HFNC in such patients due to aerosol generation. However, studies have showed that NIV and bag-mask ventilation increased the risk of transmission while high flow oxygen therapy did not and HFNC did not increase the risk of bacterial or viral transmission. HFNC is easier to implement and manage and easy to titrate than NIV and mechanical ventilation. Monitoring is less intensive, thus reducing the nursing care workload. Non-clinician workers can also operate it due to the simplicity of its use.

Another approach can be tried to improve oxygenation in patients using HFNC i.e by use of awake prone positioning. Awake pruning technique is effectively used in patients on HFNC as a respiratory support and is found to be extremely beneficial in COVID-19 infection. A study was done by Despres et al for evaluation of prone position along with high flow device or standard oxygen devices in critically ill patients of COVID-19 and it was concluded that prone positioning can be extremely beneficial in spontaneously breathing coronavirus affected patients for avoiding endotracheal intubation. There is minimal risk of skin breakdown and stability of cannula is ensured in comparison with conventional flow face masks.

HFNC can be used in claustrophobic patients who do not tolerate NIV. A study was done by Wang et al to evaluate the experience of high flow nasal device in hospitalized COVID-19 pneumonia patients in China, by retrospective screening of confirmed patients. The study indicated that HFNC was the most common and better tolerated ventilation support for COVID-19 patients.

DRAWBACKS OF HFNC
All bedside healthcare workers caring for COVID-19 are at higher risk of contracting the infection. The aerosol generating procedures or therapies can release the virus into air, thus increasing the risk of transmission. The risk of bio-aerosol dispersion has been shown with the use of conventional oxygen therapies and with the use of NIV and Mechanical ventilation too. The scientific evidence after various clinical researches has suggested that generation of aerosol and its dispersion via HFNC has a similar rate as other standard oxygen masks. Therefore, recommendation of wearing a surgical mask in patients on HFNC therapy over the nasal cannula has been suggested to reduce the spread of the virus, along with the use of personal protective equipment’s (PPE) by all healthcare professionals caring for such patients. Use of negative pressure rooms is also considered desirable but not essential when HFNC is used in COVID-19 patients. Use of a snug fit nasal
cannula also reduces the risk of aerosol dispersion; while turning off the flow when adjusting the cannula helps in further reduction. A study done by Montiel et al.\textsuperscript{54} in which use of surgical mask above the nasal cannula device was evaluated and they concluded that it increased oxygenation in severely ill patients of coronavirus disease with respiratory failure. HFNC is a little bit more expensive than standard oxygen face masks and other low flow devices which affects its use in low profile hospital settings.

Some minor drawbacks observed are nasal mucosa irritation, runny nose, alteration of smell, noise, easy dislocation of the cannula etc. But major drawback is the potential for delaying the intubation when clinically indicated, leading to poor outcomes\textsuperscript{55}. The comfort level provided by the HFNC might delay the onset of respiratory distress and confound the analysis of patient’s status by physician. Timely assessment of respiratory failure during HFNO therapy is critical. For predicting the failure of HFNO therapy, a Respiratory rate oxygen index (ROX) was developed.

ROX Index is a formula to assess the failure or success of HFNC. Roca et al.\textsuperscript{56} proposed this ROX Index for patients having acute respiratory failure. It is defined as the ratio of SpO2/FiO2 to the respiratory rate. Index value of more than 4.88 after 12 hours of HFNC treatment suggests less chances of failure of therapy and thus, lesser need of mechanical ventilation. Modified ROX Index is defined as the ratio of SpO2/FiO2 to the respiratory rate divided further by heart rate and multiplied by a factor of 100. This ROX-HR Index value of more than 6.80 means lesser chance of failure of HFNC therapy. An observational study was done for prediction of outcomes of HFNC treatment by Goh et al.\textsuperscript{57}, in which 145 patients with pneumonia were enrolled. Evaluation was done using modified ROX index and cutoff values were suggested for assessment of HFNC failure. It was observed that HFNC showed a lower ROX index overall and modified ROX index of more than 8 after 10 hours was considered as lower risk value for failure of HFNC. The study established this index as a promising method for treatment failure prediction. Other predictors\textsuperscript{58} of HFNC failure include age of the patient, presence of co-morbidities such as hypertension, diabetes mellitus type-2, obesity, duration of respiratory symptoms, steroid treatment, CRP levels, D-dimer levels, lymphocyte count etc.

Currently, clinical assessment and judgement are still the best means to identify the patients who might need mechanical ventilation after HFNC\textsuperscript{56}. An observational study including 122 patients of confirmed coronavirus disease showing respiratory failure was done and patients received either HFNC or early intubation in ICU. The HFNC use reduced the total ICU stay duration. Intubation and mechanical ventilation should be done when patients show persistent signs and symptoms of respiratory failure and meet two of the given criteria, after ruling out the failure of the equipment\textsuperscript{60}:

1) Respiratory Rate of more than 40 per minute
2) No improvement in breathing workload
3) Increased secretions with reduced clearance
4) Respiratory acidosis with pH less than 3.5
5) Saturation level i.e SpO2 of less than 90 % for a minimum of 5 minutes

**CONCLUSION**

COVID-19 has brought up many changes and challenges all over the world and in healthcare system. Hypoxemic patients are treated in ICU by healthcare teams using all possible oxygen support therapies. HFNC has been found to be a better alternative than standard oxygen therapies in COVID-19 infection. HFNC is a relatively valuable tool when used appropriately to fight the hypoxemic failure. It provides several physiological benefits that make it an effective treatment modality when compared to other oxygen therapy approaches. Its use may prevent the need of higher and more expensive and invasive interventions needed in COVID-19 treatment. The beneficial effects of HFNC in the times of coronavirus pandemic should be properly assessed and balance must be made with transmission of risk of infection to healthcare professionals along with other patients. Further studies will help to guide the role of HFNC to
deliver best and optimal device settings and duration of therapy with appropriate patient selection and to help in setting up definitive guidelines to maximize its potential.

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How To Cite This Article:

Source of Support: Nil
Conflict of Interest: None declared

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