High-Flow Nasal Cannula Oxygen Therapy in Adult Acute Care: Beyond Clinical Indications and Patient Selection

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INTRODUCTION

Oxygen therapy has been used for centuries to support patients with breathing difficulties.[1] Historically, oxygen therapy primarily involved using low-flow delivery devices. The long-term use of nasal high-flow oxygen was not common until more recently, as concerns about patient discomfort were associated with a lack of humidification. High-flow nasal cannula (HFNC) oxygen therapy refers to delivering heated and humidified gases at flows (between 20–60 L/min) through the nose to support patients in hypoxemic and/or hypercapnic respiratory failure. Over a relatively short period, HFNC oxygen therapy has become widely used in respiratory medicine. Much of its popularity comes from its ease of application, and the comfort it provides to patients. While evidence is still evolving regarding clinical indications and patient selection for HFNC oxygen therapy, other factors might play a role in the success of the modality. Thus, this feature article highlights important clinical and technical considerations of HFNC oxygen therapy.

CLINICAL APPLICATIONS

Among all the available oxygen therapy modalities, evidence suggests that HFNC oxygen therapy is superior in improving outcomes of patients with acute hypoxemic respiratory failure. For example, in a small randomised controlled trial, Roca et al.[2] compared HFNC oxygen therapy with conventional oxygen therapy via face mask among patients with acute hypoxemic respiratory failure. Their study demonstrated that HFNC oxygen therapy was associated with less dyspnoea (3.8 [1.3–5.8] versus 6.8 [4.1–7.9]: p=0.001) and mouth dryness (5 [2.3–7.0] versus 9.5 [8.0–10.0]; p<0.001), and was reported to be more comfortable (9 [8.0–10.0] versus 5 [2.3– 6.8]; p<0.001) to wear by the subjects. Additionally, HFNC oxygen therapy led to lower respiratory rates (21 [18–27] versus 28 [25–32]; p<0.001) and higher arterial blood oxygen (mmHg) levels (127 [83–191] versus 77 [64–88]; p=0.002).

A meta-analysis by Rochwerg et al.[3] reported that use of HFNC oxygen therapy, when compared with conventional oxygen therapy, lowers the risk for endotracheal intubation (risk ratio [RR]: 0.85; 95% confidence interval [CI]: 0.74–0.99) in patients with acute hypoxemic respiratory failure, but does not impact the mortality rate (RR: 0.94; 95% CI: 0.67–1.31; moderate certainty).[3]

A recent meta-analysis by Pitre et al.[4] assessed the effectiveness of non-invasive oxygen strategies for treating acute hypoxemic respiratory failure and demonstrated with moderate certainty that HFNC oxygen therapy reduces the need for invasive mechanical ventilation (103.5 fewer events per 1,000; 95% CI: 40.5–157.5 fewer). In a meta-analysis by Li et al.[5] compared HFNC oxygen therapy with conventional oxygen therapy, similar findings were reported, but their analysis showed a decrease in 28-day intensive care unit mortality rates (odds ratio: 0.54; 95% CI: 0.30–0.97; p=0.04) with the use of HFNC t herapy among adult patients with acute respiratory failure secondary to COVID-19.[5]

When comparing the clinical effectiveness of HFNC oxygen therapy to non-invasive ventilation (NIV), a meta-analysis by Beran et al.[6] reported no difference in the intubation rate (RR: 1.01; 95% CI: 0.85–1.20; p=0.89), but improvement in the mortality rate (RR: 0.81; 95% CI: 0.66–0.98; p=0.03) among patients with COVID-19 with the use of NIV.[6] Amidst the COVID-19 pandemic, non-invasive respiratory support, especially HFNC oxygen therapy, was extensively utilised to manage patients with acute respiratory failure secondary to COVID-19.[7] This approach helped decrease the requirement for invasive mechanical ventilation, subsequently alleviating the strain on the availability of ventilators.

When assessing the impact of HFNC therapy on hypercapnic respiratory failure, the existing evidence indicates a reduction in arterial CO_2 level among patients with stable chronic obstructive pulmonary disease (COPD).[8,9] A physiologic study by Rittayamai et al.[10] enrolled 12 patients with hypercapnic COPD demonstrated that HFNC oxygen therapy use at a flowrate of 30 L/min provides similar clinical effect as NIV. A recent randomised controlled trial by Nagata et al.[11] reported that the home use of HFNC oxygen therapy among patients with stable hypercapnic COPD resulted in a significant lower rate of moderate/severe exacerbations as compared with the conventional oxygen therapy (mean count 1.0 versus 2.5). Overall, the majority of the evidence available have demonstrated that using HFNC oxygen therapy to manage acute hypoxemic respiratory failure yields better patient outcomes when compared with conventional oxygen therapy; however, its application produces similar outcomes when compared with the NIV. The available data supports the adoption of HFNC oxygen for treating chronic hypercapnic respiratory failure, but its role in managing acute hypercapnic respiratory failure is currently unknown.

PHYSIOLOGICAL EFFECTS OF HIGH-FLOW NASAL CANNULA

The major physiologic effects of HFNC oxygen therapy include the washout of anatomical dead-space, a 'more stable' delivery of fraction of inspired O_2 (F_IO_2), adequate heating and humidification of inspired gases, and positive pressure. Washing out CO_2 from the anatomical dead space improves gas exchange efficiency. This is because a more significant portion of the minute volume is actively involved in gas exchange.[12] During HFNC oxygen therapy, the device can deliver flows that exceed patient peak tidal inspiratory flow (PTIF). When the PTIF is exceeded, it reduces the risk of diluting the delivered F_IO_2 through the entrainment of ambient air. Patients have control over their PTIF and tidal volume, so there is likely some variability in the delivered F_IO_2.[12,13] Providing properly warmed and humidified gases offers several benefits, including improved mucociliary function, enhanced clearance of secretions, reduced airway constriction, and decreased metabolic costs of breathing.[14-16] Finally, despite being an open system, HFNC oxygen therapy devices provide some positive pressure. Evidence has shown that pharyngeal pressures and end-expiratory lung volumes increase with HFNC oxygen therapy. Improved gas exchange can result from the increased alveolar recruitment due to the positive pressure generated; however, an open mouth during patient breathing complicates the positive pressure effect. Studies exploring the impact of mouth closure or openness have demonstrated considerable variation in pharyngeal pressures. Factors such as BMI, lung heterogeneity, and device flow rate may also contribute to the variability in lung recruitment observed with HFNC oxygen therapy.[15,17–21]

HIGH-FLOW NASAL CANNULA SETTINGS

Flow settings impact the aforementioned physiologic effects of HFNC oxygen therapy. Surpassing the PTIF appears to maximise the benefits of HFNC oxygen therapy, if the flows do not cause patient discomfort and alveolar overdistension.[22,23] However, clinicians currently face the challenge of having no commercially available device to measure PTIF directly. Furthermore, variations in PTIF occur due to patient and disease conditions, further complicating the matter.[23] Without a PTIF measurement device or tool, clinicians must rely on clinical indicators to establish and adjust patient flows.

A systematic review conducted by Li et al.,[23] which assessed the impact of flow settings, suggested that until a PTIF measurement device becomes available, clinical findings such as patient comfort, respiratory rate and oxygenation (ROX) index, respiratory rate, and oxygenation should be utilised to personalise flow settings. This approach might help individualise and optimise flow settings without a direct PTIF measurement device.[24]

Patient comfort cannot be overstated, as the success of the therapy relies on patient compliance. In a prospective, randomised, cross-over study by Mauri et al.,[25] patient comfort appeared to be affected by temperature. A temperature of 31 °C was more comfortable than 37 °C at both 30 and 60 L/min ($p<0.0001$). Interestingly, the authors reported that in a subgroup of patients (those with a F_IO_2 >0.45), a temperature of 31 °C, and a flow of 60 L/min led to higher comfort ($p<0.01$). While it may be intuitive that higher flows may decrease comfort, this may not be true, at least for some patients. Clinicians should make efforts in adjusting heat and flow settings (in addition to a properly fitted nasal interface) to maximise patient comfort during HFNC oxygen therapy.

AEROSOL DELIVERY VIA HIGH-FLOW NASAL CANNULA

Patients with acute respiratory failure often receive aerosol therapy in addition to the HFNC oxygen therapy. However, delivering aerosolised medications via HFNC is a relatively new technique. Traditional oxygen delivery methods require a stoppage in the therapy to be able to administer aerosolised medications. The advantages of delivering aerosol delivery via HFNC is that it allows clinicians to provide uninterrupted respiratory support to the patients.[26] During HFNC oxygen therapy, aerosol particles are generated by nebulisers and get entrained within the high gas flow and carried to patient lungs. To optimise aerosol delivery through a HFNC device, clinicians should consider nebuliser type (jet or vibrating mesh), nebuliser placement, and gas flow.[26] A study by Dugernier et al.[27] compared aerosol delivery between jet nebuliser and vibrating mesh nebuliser through a HFNC, and found that vibrating mesh nebuliser yielded a three-times higher lung deposition as compared to the jet nebuliser. Similarly, a bench study by Li et al.[28] demonstrated that use of vibrating mesh nebuliser resulted in a higher inhaled dose as compared with the small volume jet nebuliser. Another study by Li et al.[29] studied the impact of nebuliser placement on the aerosol delivery, and reported that a nebuliser placed at the humidifier level resulted in higher inhaled dose as compared to a nebulizer placed close to the patient. Lastly, the set gas flow rate of HFNC also influences the drug deposition. HFNC device gas flow is generally set at a higher rate (40–60 L/min) to meet the PTIF to maximise the physiologic effects of the modality. Alcoforado et al.[30] studied the effect of HFNC flow on drug deposition and reported that lung deposition was greater for 10 L/min flowrate, as compared with 30 L/min or 50 L/min (17.2±6.8%, 5.71±2.04%, and 3.46±1.24%, respectively; $p=0.0001$).[29] To achieve higher lung deposition when administering aerosol therapy via HFNC, it may be advantageous to use a vibrating mesh nebuliser placed close to the humidifier, and utilise lower flowrates on the device. More studies are needed to determine precisely which flows are best on the various devices that are commercially available.

CONCLUSION

HFNC oxygen therapy is a commonly used respiratory intervention to support patients with acute respiratory failure. To achieve maximum clinical benefits, clinicians need to look beyond clinical indications of the modality, and consider how settings and medication delivery strategies play a role in improving outcomes. More studies are needed, particularly in exploring the application of HFNC oxygen in addressing hypercapnic respiratory failure, as the use of the modality increases, and the technology evolves.

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