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Heated Humidified High-Flow Nasal Oxygen in Adults

Mechanisms of Action and Clinical Implications

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Traditionally, nasal oxygen therapy has been delivered at low flows through nasal cannulae. In recent years, nasal cannulae designed to administer heated and humidified air/oxygen mixtures at high flows (up to 60 L/min) have been gaining popularity. These high-flow nasal cannula (HFNC) systems enhance patient comfort and tolerance compared with traditional high-flow oxygenation systems, such as nasal masks and nonrebreathing systems. By delivering higher flow rates, HFNC systems are less apt than traditional oxygenation systems to permit entrainment of room air during patient inspiration. Combined with the flushing of expired air from the upper airway during expiration, these mechanisms assure more reliable delivery of high F_{IO_2} levels. The flushing of upper airway dead space also improves ventilatory efficiency and reduces the work of breathing. HFNC also generates a positive end-expiratory pressure (PEEP), which may counterbalance auto-PEEP, further reducing ventilator work; improve oxygenation; and provide back pressure to enhance airway patency during expiration, permitting more complete emptying. HFNC has been tried for multiple indications, including secretion retention, hypoxemic respiratory failure, and cardiogenic pulmonary edema, to counterbalance auto-PEEP in patients with COPD and as prophylactic therapy or treatment of respiratory failure postsurgery and postextubation. As of yet, very few high-quality studies have been published evaluating these indications, so recommendations regarding clinical applications of HFNC remain tentative. CHEST 2015; 148(1):253-261

ABBREVIATIONS: ACPE = acute cardiogenic pulmonary edema; DNI = do not intubate; HFFM = high-flow face mask; HFNC = high-flow nasal cannula; NIV = noninvasive ventilation; PEEP = positive end-expiratory pressure; SBT = spontaneous breathing trial; Sp_{O_2} = oxygen saturation as measured by pulse oximetry

Oxygen therapy is the first line of treatment in patients with hypoxemia and may be delivered using low-flow devices (up to 15 L/min), such as nasal cannulae, nonrebreathing masks, and masks with reservoir bags. These deliver varying levels of F_{IO_2} depending on the patient's breathing pattern, peak inspiratory flow rate, delivery system, and mask characteristics.[1,2] Maximal flow rates with these devices are limited partly by

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their inability to effectively heat and humidify gas at high flow rates. Conventional high-flow systems, such as Venturi masks, use a constant flow of oxygen through precisely sized ports and, through steady entrainment of room air using the Bernoulli effect, provide a more constant F_{IO_2} than conventional nasal systems.[1-3] However, these systems are less well tolerated than nasal cannulae due to obtrusiveness of the masks and insufficient heating and humidification of the inspired gas.[1-3] Additionally, at high patient inspiratory flow rates, entrained room air dilutes the oxygen and lowers F_{IO_2}.

Over the past 2 decades, systems to deliver heated and humidified oxygen at high flows through nasal cannulae have been developed as an alternative to standard oxygen delivery systems. A high-flow nasal cannula (HFNC) delivers a flow rate up to 8 L/min in infants and 60 L/min in adults. The device consists of an air/oxygen blender connected through an active heated humidifier to the nasal cannula and allows adjustment of the F_{IO_2} independently from the flow rate.

HFNC was first used in preterm neonates and pediatric care. In this population, its role has been and is still being extensively studied as a first-line treatment in respiratory distress syndrome, in apnea of prematurity, and in the postextubation period to prevent extubation failure. Some authors have proposed the use of HFNC in neonates as an alternative to CPAP because as opposed to standard oxygen therapy, it can also generate positive end-expiratory pressure (PEEP) and is better tolerated as a result of the heating and humidification.[4]

More recently, anecdotal case reports, case series, and some preliminary controlled trials have drawn attention to the potential role of HFNC in adults owing to its ability to set and deliver a desired F_{IO_2}, its better tolerance compared with standard face masks, and its avoidance of desiccation, which enhances comfort and secretion mobilization. In this narrative review, we critically examine the current literature focusing on the proposed mechanisms of action, clinical benefits, and potential applications of HFNC in adults receiving acute care; compare this approach to conventional oxygen supplementation and noninvasive ventilation (NIV); and highlight the many knowledge gaps requiring further study.

Search Criteria

We searched for publications and abstracts on PubMed, the Cochrane Database of Systematic Reviews, and Scopus using the search terms “high flow” OR “humidified” OR “heated” AND “oxygen therapy” OR “nasal oxygen.” We limited the search to English-language publications but did not limit the search based on publication type. We searched for both bench studies and adult human studies. We considered only studies defining nasal high flow as a flow rate ≥ 20 L/min.

Potential Mechanisms of Clinical Benefit

HFNC consists of high-flow gas with an F_{IO_2} ranging from 0.21 to nearly 1.0 adjusted by an oxygen blender, brought to body temperature, and saturated with water through an in-line humidifier. The gas mixture is then provided to the nares through loose-fitting nasal prongs that are slightly larger but softer than those used for standard nasal oxygen therapy. The mechanisms by which HFNC may offer advantages to patients with dyspnea and hypoxemia are shown in Table 1.

Favorable Effects of Heated and Humidified Gas

Effects on Comfort and Tolerance: Traditional methods of oxygen delivery provide nonhumidified or underhumidified gas that dries the upper airway, interferes with mucociliary clearance, facilitates atelectasis, and ultimately reduces patient comfort and tolerance. Little evidence is available on the beneficial effects of humidification when low-flow oxygen is supplemented, but with conventional higher-flow oxygen (up to 15 L/min) through face masks, tolerance is reduced by inhalation of cold, dry gas, even when a bubble humidifier is used.[3,25] In a crossover study in 20 patients with acute respiratory failure mainly due to pneumonia, Roca et al[5] found that compared with face mask oxygenation using a bubble humidifier, HFNC was associated with greater overall comfort, lower dyspnea scores, and reduced mouth dryness.

In other studies of patients postextubation, a favorable trend in comfort and tolerance was observed in patients on HFNC compared with conventional oxygen therapy.[6,7] In contrast, Parke et al[26] found that HFNC was less well tolerated than conventional oxygen therapy in the postextubation period after cardiac surgery. However, the study population was more stable than in the other studies and may not have had conditions likely to benefit from HFNC. On the whole, the available evidence suggests that HFNC enhances comfort and tolerance in patients with respiratory distress, but more work is needed to determine how to best select candidates and make adjustments (airflow, levels of heat and humidity) to optimize comfort.

TABLE 1] Potential Mechanisms of Clinical Benefit During HFNC Use

Mechanism	Clinical Benefit
Small, loose-fitting nasal prongs	Enhanced comfort[5-7]
Heat and humidification	Enhanced comfort[5-7]
Increased water content of mucus	Facilitated secretion removal Avoidance of desiccation and epithelial injury[8,9]
Decreased metabolic cost of breathing	Reduced work of breathing[10,11]
High nasal flow rate	Reduced inspiratory entrainment of room air if mouth closed; more reliable delivery of F_{IO_2}[12-14]
Washout of upper airway dead space	Improved efficiency of ventilation[15-17] Enhanced oxygen delivery[18]
PEEP[12,19-24]	Counterbalance auto-PEEP Decreased work of breathing

HFNC = high-flow nasal cannula; PEEP = positive end-expiratory pressure.

Effects on Secretion Characteristics and Mobilization: Patients with respiratory distress and failure commonly have increased airway secretions and expend considerable effort expelling them. This effort could contribute to respiratory muscle fatigue and progression of respiratory failure, especially when secretions become thick and difficult to mobilize. This is not an uncommon occurrence during NIV when instances of mucus retention have been reported.[27]

Water content of mucus affects viscosity and plays an important role in the transport of secretions. Physiologic humidification of secretions depends on proper functioning of airway epithelial cells through Na^+ absorption and Cl^- secretion. Breathing dry gas is dessicating, damaging epithelial cells and altering the characteristics of mucus.[8] Proper humidification is, therefore, needed to preserve and optimize mucosal functions, including facilitating gas exchange, limiting the metabolic cost of breathing, and maintaining host defenses.[28]

Warming inspired gas to the level of core temperature (37°C) and humidifying it to saturation help to maintain adequate mucosal function and preserve the rheology and volume of secretions, maximizing mucociliary clearance without risk of thermal injury or over-humidification.[8] Deviation from these optimal conditions interferes with ciliary function and mucus transport, as shown by reductions of both ciliary beat frequency and mucus transport velocity after exposure to lower temperatures (34°C and 30°C).[29,30]

By virtue of its ability to hydrate airways, HFNC was first envisioned as a modality to facilitate secretion removal in patients with bronchiectasis.[9] Thus, in conditions characterized by the need for adequate secretion removal (ie, pneumonia, COPD, cystic fibrosis, acute and chronic bronchitis, bronchiectasis), HFNC could be quite helpful.

Reduction in the Metabolic Cost of Breathing: The delivery of warmed and humidified gas not only enhances comfort for the patient but also avoids desiccation of the nose and upper airways and therefore may help to avoid the bronchoconstricting effect of cold, dry gas.[10] The metabolic cost necessary to warm and increase the relative humidity of inspired gas is not negligible, especially in patients with tachypnea and acute respiratory failure.[11] Reducing this metabolic component of the work of breathing could potentially be beneficial for patients. Furthermore, by maintaining the integrity of mucociliary function and rendering secretions easier to mobilize, HFNC might also reduce the energy expended with expectoration. However, these "energy-saving" effects of HFNC and their impacts on outcomes in patients with respiratory failure are largely speculative and remain to be better understood.

High Flow Rate Minimizes Entrainment of Room Air

Patients in respiratory distress often have high inspiratory flow rates that substantially exceed the flow rates of standard oxygen delivery systems.[1] Entrained room air dilutes the supplemental oxygen, often substantially reducing delivered F_{IO_2}. HFNC generates a higher flow rate compared with other oxygen delivery systems, exceeding the patient's peak inspiratory flow rate in most cases. As a consequence, less mixing with room air occurs, and the desired F_{IO_2} is more reliably delivered.[12-14]

However, open-mouth breathing during HFNC lowers delivered F_{IO_2} compared with closed-mouth nasal breathing due to mixing of the high-flow nasal oxygen with room air inhaled through the mouth.[13] Additionally, peak inspiratory flow rate may rise to > 90 L/min during exercise, exceeding the flow capabilities even of HFNC, so that entrained room air may substantially lower delivered F_{IO_2}.[13] Nonetheless, HFNC is likely to perform better under these circumstances than traditional oxygen supplementation.

Increase in Ventilatory Efficiency

Washout of Nasopharyngeal Dead Space: The ability to continually flush out CO_2 from the upper airway is another potential benefit of HFNC.[15-17] Similar to tracheal gas insufflation,[31] this would eliminate dead space attributable to the flushed-out volume, permitting a higher fraction of minute ventilation to participate in gas exchange.[32] Using a bench model of the nasal cavity to assess the fluid dynamics of gas during both simulated spontaneous breathing and use of HFNC, Spence et al[33] demonstrated that the flow pattern of gas in the nasopharynx was significantly altered by HFNC. In particular, gas recirculation flushes CO_2 from the nasopharynx during HFNC use, reducing the fraction of inspired CO_2 and raising F_{IO_2}.[18] Frizzola et al[34] reported the same effect in a piglet model of acute lung injury, showing that the washout of anatomic dead space was related more to the incremental flow than to the incremental pressure. These effects would be expected to improve the efficiency of ventilation and efficacy of oxygen delivery compared with standard oxygen delivery systems. The evidence suggests greater effects at higher flow rates, but precisely how much dead space can be flushed out at high nasal flow rates in patients with respiratory failure remains to be determined.

PEEP Effect: Multiple studies on infants and neonates have shown that HFNC significantly elevates naso-pharyngeal or esophageal pressure, approximating levels seen with nasal CPAP. Because of air leakage though, the pressure levels are quite variable.[19-22] In 2007, Groves and Tobin[23] were the first to demonstrate that HFNC systems also generate positive expiratory pharyngeal pressure in adults. The airway pressure recorded during spontaneous breathing with HFNC correlates linearly with the administered flow rate and is significantly higher when subjects breathe with their mouths closed.[23] These results have been confirmed in healthy volunteers[12,23] and in patients with stable COPD and idiopathic pulmonary fibrosis[24] and postcardiac surgery.[35-37] Parke et al[37] observed that for each increase of 10 L/min in flow rate, mean airway pressure increased by 0.69 cm H_2O ($P < .01$) when subjects breathed with their mouths closed and by 0.35 cm H_2O ($P < .03$) when they breathed with their mouths open. Another study by the same group showed that pressure generated by HFNC peaks at end expiration (Fig 1).[38]

Low-level positive airway pressure is also generated by HFNC during inspiration, unrelated to the amount of mouth closure during breathing.[23,37] Even though this finding suggests a role of HFNC in reducing the work of breathing by providing a small amount of inspiratory assistance and counterbalancing auto-PEEP through the aforementioned end-expiratory pressure effect, especially in patients with COPD, no direct measurements of the effects of HFNC on respiratory muscle function have yet been reported. Therefore, conclusions about the effect of HFNC on the work of breathing, especially in patients with various etiologies for respiratory failure, must await more definitive investigations.

Effects on Breathing Pattern: In healthy volunteers, HFNC alters the breathing pattern through an increase in tidal volume and reduction in respiratory rate, with minute volume remaining steady.[39,40] Using electrical impedance tomography, Corley et al[36] observed the same increase in tidal volume in postcardiac surgery patients. Tidal volume and end-expiratory lung volume increased the most in patients with a higher BMI. Such alterations in breathing pattern and lung volumes could reproduce the favorable effects of CPAP in patients with acute pulmonary edema, opening of flooded alveoli with improved oxygenation, and lung compliance as well as reduced left ventricular afterload.[41-43] But whether the pressure elevations with HFNC are sufficient to realize these benefits has not yet been established.

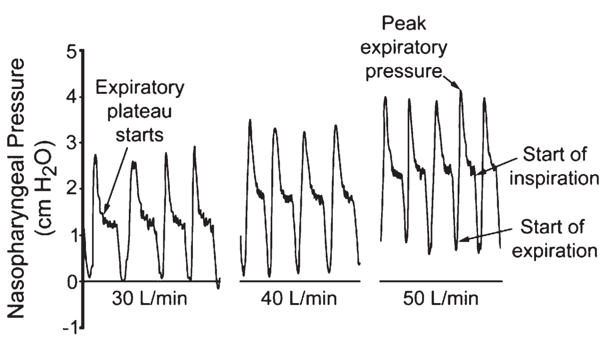

Figure 1 – *Nasopharyngeal pressure generated by high-flow nasal cannula oxygen during the respiratory cycle at various flow rates in one patient postcardiac surgery. (Reprinted with permission from Parke and McGinness.[38])*

Potential Clinical Applications

Hypoxemic Respiratory Failure

HFNC has been tried in a number of different types of hypoxemic respiratory failure (Table 2). Initially, a few anecdotal cases were reported on the comfort and oxygenation advantages of HFNC in respiratory failure and during procedures such as bronchoscopy in patients with hypoxemia.[44,49-51] Two retrospective analyses showed significant improvement in oxygenation and reduction in respiratory rate in adult burn patients[52] and in a surgical high-dependency unit.[53]

In 2010, Roca et al[5] reported the first prospective crossover intervention study in acute respiratory failure comparing HFNC to conventional oxygen delivery through high-flow face mask (HFFM) combined with nasal cannula (sum of face mask and nasal cannula flow, 20 L/min). In 20 patients, comfort, tolerance, and oxygenation were all better with HFNC than with HFFM at the same targeted F_{IO_2} of 50% (Pa_{O_2}, 127 mm Hg vs 77 mm Hg; $P = .002$), with no significant difference in pH or Pa_{CO_2}. Sztrymf et al[16] confirmed the favorable effects of HFNC on oxygenation as well as significantly lower respiratory (24.5/min vs 28/min, $P < .006$) and heart rates at 1 h compared with HFFM. These authors identified failure of respiratory rate to drop, lower oxygen saturation, and persisting thoracoabdominal asynchrony as predictors of HFNC failure (nine of the 38 subjects needed intubation and mechanical ventilation).[15]

Most studies on HFNC in patients with hypoxemia have been conducted in an ICU or high-dependency unit. Lenglet et al[17] examined HFNC use in patients with hypoxemia in the ED. After 15 min, HFNC improved oxygen saturation as measured by pulse oximetry (Sp_{O_2}) (96% vs 90%, $P < .01$), respiratory rate (25/min vs 28/min), and dyspnea scores (both Borg and a 10-point visual analog scale) compared with baseline values. An accompanying survey of ED providers found that 75% preferred HFNC over standard oxygen therapy.[17]

In a recent prospective but uncontrolled trial in 28 patients with hypoxemic respiratory failure, excluding those with acute cardiogenic pulmonary edema (ACPE), Frat et al[45] applied HFNC sequentially with NIV (2 h alternating with 1 h, respectively) and found that HFNC improved oxygenation compared with standard oxygen therapy but not as much as NIV. HFNC also reduced respiratory rate compared with standard oxygen therapy and was better tolerated than NIV. Ten patients (36%) required intubation, and a respiratory rate $\geq$ 30/min after initiation of HFNC predicted the need for intubation. Despite these promising results, we await the completion of several large, multicenter randomized trials currently under way to adequately assess oxygenation capabilities compared with standard oxygen therapy and NIV and to determine the types and severities of hypoxemic respiratory failure most likely to benefit from HFNC.

Acute Cardiogenic Pulmonary Edema

By virtue of its ability to oxygenate effectively and provide low levels of PEEP, HFNC has been proposed as a therapy for ACPE. Like CPAP, HFNC is hypothesized to open

TABLE 2] Potential Clinical Applications of High-Flow Nasal Oxygen

Application	Benefits
Procedures	Enhanced oxygenation during endoscopy[44]
Hypoxemic respiratory failure	
ARDS	Mild and early[45]
Pneumonia	Enhanced oxygenation[5,16]
Idiopathic pulmonary fibrosis	Lower respiratory rate[24]
Cardiogenic pulmonary edema	Enhanced oxygenation Reduced dyspnea[45]
Postoperatively	
Cardiothoracic and vascular	Improved thoracoabdominal synchrony[46]
Cardiac surgery	Increased end-expiratory lung volume[36] Less escalation of therapy[26]
Postextubation	Improved oxygenation and ventilation[47] Enhanced comfort[6,7] Less displacement of interface[47] Less escalation of therapy to noninvasive ventilation or intubation[47]
Do-not-intubate patients	Improved oxygenation and respiratory mechanics[48]

flooded alveoli, improving lung compliance and oxygenation while enhancing cardiac function through the afterload-reducing effect of the end-expiratory pressure. In a cohort of five patients with persisting hypoxemia and dyspnea on conventional oxygen therapy after treatment of ACPE with NIV, HFNC significantly improved arterial blood gases (P_{O_2} and pH) and reduced dyspnea.[54] Randomized controlled trials on the use of HFNC as a treatment in patients with ACPE are needed.

Postoperative Patients

Postcardiothoracic and Vascular Surgery: In a preliminary randomized trial of 60 patients with mild to moderate acute hypoxemic respiratory failure following cardiothoracic or vascular surgery, Parke et al[46] found that patients treated with HFNC had a lower failure rate (defined as escalation to NIV) than those receiving HFFM ($P = .006$) and had fewer oxygen desaturations. Use of NIV in the two groups was not significantly different, but five of the failures in the face mask group were crossed over to HFNC, of whom only one required NIV. Although the results favored HFNC, the small sample size, use of HFNC as an escalation therapy from face mask, and lack of protocolized criteria for escalation in an unblinded study limited the conclusions.

A more recent prospective study in 40 patients with hypoxemic respiratory failure, most of whom were postoperative, showed improved thoracoabdominal synchrony with HFNC compared with low-flow-mask oxygen delivery (up to 8 L/min).[47] Oxygenation was not better in the HFNC group than the low-flow oxygen group, but the study was small, and most patients had only mild respiratory failure and may not have been sufficiently hypoxemic to manifest a significant benefit.[47]

Postcardiac Surgery: Corley et al[36] found in a cohort of 20 patients with respiratory dysfunction that HFNC reduced respiratory rate and Borg dyspnea score and improved oxygenation compared with baseline measures. In addition, HFNC increased airway pressure and end-expiratory lung volume as determined by electrical impedance tomography, especially in patients with a higher BMI. The authors speculated that HFNC could play a useful role in postcardiac surgery in patients who are obese or intolerant of NIV.[36]

Parke et al[26] randomized 340 patients undergoing elective cardiac surgery, including sternotomy and cardiopulmonary bypass, to postoperative prophylactic use of HFNC or standard oxygen therapy. They found no significant difference in Sp_{O_2} or F_{IO_2} on days 1 to 3 after surgery. Furthermore, HFNC did not reduce atelectasis or ICU length of stay. HFNC did lower the need for escalation to NIV or intubation (27.8% vs 45% of patients, $P < .001$). Further trials are needed to assess the possible role of HFNC to avoid pulmonary complications or escalation of therapy in postcardiac surgical and other postoperative settings, especially in higher-risk populations.

Postextubation

Patients recently extubated are prone to oxygen desaturations and often require standard high-flow oxygen therapy; therefore, it is reasonable to hypothesize that HFNC is useful for these patients. Two randomized crossover trials compared short-term interventions (30-min HFNC vs 30-min HFFM) in patients extubated after passing a spontaneous breathing trial (SBT).[6,7] Both studies showed a trend toward better comfort with HFNC and no significant difference in gas exchange. However, the results of the two trials were conflicting, with one[6] reporting no differences between treatments and the other[7] finding reductions in dyspnea score (1.6 vs 2.9, $P = .04$), respiratory rate (19.8/min vs 23.1/min, $P = .009$), and heart rate (89.5/min vs 95.4/min, $P = .006$) with HFNC compared with HFFM. This discrepancy could be explained by the different protocols used in the two studies. In the former, subjects were randomized to the first intervention 30 min after extubation, and the HFFM flow rate was ≥ 30 L/min. In the latter, the randomization happened immediately after extubation, and the HFFM flow rate was only 6 to 8 L/min.

A more recent randomized trial[55] compared HFNC to Venturi masks in 105 patients intubated for at least 24 h and extubated after passing an SBT but having a $Pa_{O_2}/F_{IO_2} \leq 300$ at the end of the SBT. If patients had failed more than three SBTs, were hypercapnic ($Pa_{CO_2} > 45$ mm Hg), or had a respiratory rate > 25/min just before the SBT, they received NIV and did not undergo randomization. The HFNC group had a significantly better oxygen saturation and Pa_{O_2}/F_{IO_2} and a lower respiratory rate than those randomized to the Venturi mask. The P_{CO_2} and discomfort related to the interface and dryness were also lower in the HFNC group. Furthermore, HFNC was associated with fewer episodes of interface displacement and oxygen desaturation and less need for escalation to NIV or reintubation. These promising results seem to justify the use of HFNC in the postextubation setting, but how to select patients most likely to benefit and when to apply it in relation to conventional oxygen techniques and NIV deserve further study.

Do-Not-Intubate Patients and Palliative Care

Another possible indication for HFNC is as a palliative treatment of hypoxemia and respiratory distress in do-not-intubate (DNI) patients. In this population, HFNC is an alternative to standard NIV, which would otherwise add to discomfort and interfere with speaking and eating.[56] In a retrospective analysis of HFNC in DNI patients with cancer and respiratory distress, Epstein et al[48] found that 85% of 183 patients treated with HFNC improved or remained stable. Another retrospective study involving DNI patients mainly with idiopathic pulmonary fibrosis, pneumonia, or COPD showed that HFNC improved oxygenation and respiratory mechanics, but 18% of patients still needed escalation of therapy to NIV.[57] Minimal information is available on this application of HFNC, however, and the role of HFNC among the multiple options for palliation remains to be determined.

Possible Role for HFNC in the Treatment of Hypoxemia and Respiratory Failure

Based on the multiple physiologic and subjective benefits of HFNC compared with standard oxygen therapy, HFNC is assuming a role in the management of hypoxemia and respiratory failure. The greatest benefit appears to be in patients who have severe hypoxemia and would ordinarily receive standard high-flow oxygen therapy by mask. For these patients, HFNC offers enhanced comfort, more-reliable delivery of F_{IO_2}, and more-efficient ventilation. HFNC is unlikely to benefit patients with more mild hypoxemia doing well on low-flow nasal oxygen. Additionally, although it is better tolerated than NIV and might be used in place of NIV in some patients or sequentially with NIV to provide better oxygenation and comfort during breaks from NIV, caution should be exercised in patients with high breathing workloads whose ventilatory failure is worsening. Because it generates only slight elevations of airway pressure at end expiration, HFNC is unlikely to reduce the work of breathing as effectively as NIV. Thus, HFNC is perhaps best situated in the middle of the spectrum of therapies to treat hypoxemia and respiratory failure. It supplies more oxygenation and gas flow than is necessary for patients with mild hypoxemia and not enough positive pressure or ventilator assistance for patients more severely afflicted. The advantages of HFNC over standard oxygen delivery systems are significant, and we will likely see increasing use in acute and critical care settings as more data emerge and its role becomes better defined.

Practical Application

Because of the limited clinical data available for adult applications of HFNC, it is difficult to make firm recommendations on practical aspects of HFNC use. Physiologic studies have demonstrated that the beneficial effects of HFNC are related to flow rate, so we prefer to initiate therapy by adjusting this parameter first and then to titrate the F_{IO_2} to maintain target oxygenation. Flow rates on commercially available devices range from 5 to 60 L/min. Studies in the literature have started with flow rates of 20,[5] 35,[26] and 50[57] L/min. We usually start with a flow rate of 35 L/min, which provides some PEEP and is well tolerated by most patients. Flow rate is then adjusted upward in 5 to 10 L/min increments if the respiratory rate fails to drop or breathing remains labored and downward if not tolerated. Either increasing F_{IO_2} or the flow rate would be expected to improve oxygenation, the latter because of reduced entrainment of room air during inspiration. Uptitration of flow rate is usually preferred to raising F_{IO_2} as an initial strategy to increase Sp_{O_2}, but if Sp_{O_2} falls substantially below the target level (usually > 90% to 92%), increases in F_{IO_2} can raise Sp_{O_2} more rapidly. Further increases in flow rate can then be used to maintain targeted Sp_{O_2} while F_{IO_2} is lowered to nontoxic levels ($\leq$ 60%). Patients can tolerate HFNC continuously for prolonged periods (many days) and can be weaned to standard oxygen supplementation techniques if they are oxygenated adequately on a flow rate $\leq$ 20 L/min and $F_{IO_2} \leq$ 50%. Until the safety of HFNC can be established in various settings, we recommend that HFNC use be limited to ICUs or intermediate care units where patients can be closely monitored; its use on regular wards should be discouraged, especially in patients with severe hypoxemia who are prone to severe oxygen desaturations if disconnected.

Conclusions

Devices that deliver high-flow heated and humidified oxygen through nasal cannulae (HFNCs) have become a standard of care in several clinical situations for infants, children, and preterm neonates. By virtue of a number of physiologic benefits over conventional oxygen therapy, including greater comfort and tolerance, more-effective oxygenation in some circumstances, and improved breathing pattern with increased tidal volume and decreased respiratory rate and dyspnea, we are now seeing increasing use for adults. HFNC has been used to treat hypoxemic respiratory failure and cardiogenic pulmonary edema as well as postoperatively and postextubation as both prophylaxis against pulmonary complications and treatment of frank respiratory failure. However, most of the studies addressing these applications are of low quality, limiting the ability to draw conclusions or make recommendations. Further physiologic and randomized controlled studies are needed to confirm the clinical advantages of HFNC over other methods in specific adult populations, to evaluate longer-term effects, and to determine the optimal use of HFNC in relation to other modalities, such as standard oxygen therapy and NIV.

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