High-Flow Nasal Cannula Therapy in Do-Not-Intubate Patients With Hypoxemic Respiratory Distress

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BACKGROUND: Patients with do-not-intubate (DNI) status and respiratory failure are commonly treated with noninvasive ventilation (NIV). High-flow nasal cannula (HFNC) therapy supplies a high flow of heated and humidified oxygen that may provide an effective alternative to NIV. We assessed the efficacy of HFNC in DNI patients with hypoxemic respiratory distress. METHODS: We identified 50 DNI patients with hypoxemic respiratory distress who were admitted to a medical ICU and who received HFNC. We excluded patients with P_{aCO_2} > 65 mm Hg and pH < 7.28. The primary end point was the need for escalation to NIV, as determined by the primary service. Mean changes in oxygen saturation and breathing frequency before and after HFNC were compared. RESULTS: The subjects included 25 men and 25 women, mean age 73 years (range 27–96 y). Diagnoses (allowing multiple conditions) included pulmonary fibrosis (15), pneumonia (15), COPD (12), cancer (7), hematologic malignancy (7), and congestive heart failure (3). Hospital mortality was 60% (30/50). HFNC was initiated at a mean F_{IO_2} of 0.67 (range 0.30–1.0) and flow of 42.6 L/min (range 30–60 L/min). Mean O_2 saturations went from 89.1% to 94.7% (*P* < .001), and breathing frequency went from 30.6 breaths/min to 24.7 breaths/min (*P* < .001). Nine of the 50 subjects (18%) escalated to NIV, while 82% were maintained on HFNC. The median duration of HFNC was 30 hours (range 2–144 h). CONCLUSIONS: HFNC can provide adequate oxygenation for many patients with hypoxemic respiratory failure and may be an alternative to NIV for DNI patients. *Key words: oxygen inhalation therapy; humidification; respiratory insufficiency; noninvasive ventilation.* [Respir Care 2013;58(4):597–600. © 2013 Daedalus Enterprises]

Introduction

Patients with acute respiratory insufficiency may benefit from noninvasive ventilation (NIV).[1-3] High-flow nasal cannula therapy (HFNC) supplies a high flow of heated and humidified mixed gas through a nasal cannula.[4] In addition to the ability to generate high flow and concentration of supplemental oxygen, HFNC generates a low level of positive airway pressure, especially with the mouth closed.[5,6] In hypoxemic patients, HFNC may provide effective support with greater ease of use and patient comfort than techniques requiring a tight face mask.[7]

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While the practice might be debated, patients with respiratory failure who have expressed that they not be resuscitated or intubated are commonly treated with NIV.[8] NIV may be effective in this setting, especially for those with congestive heart failure and COPD.[9,10] NIV is typically initiated in the ICU setting, so that it is common for a patient with do-not-resuscitate (DNR) or do-not-intubate (DNI) status to be admitted or transferred to the ICU specifically for consideration of NIV. For this study we sought

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to identify DNI patients with hypoxemic respiratory failure who might benefit from HFNC before proceeding to NIV, which has become common in our practice. The objectives were to assess the effectiveness of HFNC in DNI patients with hypoxemia and mild hypercapnia, the need for escalation to NIV, parameters of ventilation and gas exchange, and patient tolerance. We hypothesized that the majority of patients could be adequately supported with HFNC and avoid the use of NIV.

Methods

The study was approved by the Mayo Clinic institutional review board. Patient data were reviewed only if the subject had given consent for use of medical records for research. We reviewed the medical histories of 50 consecutive patients meeting criteria for inclusion, between May 2009 and May 2011, in the medical or medical-surgical ICU of the 2 hospitals of the Mayo Clinic in Rochester, Minnesota. The subjects were managed clinically by the primary critical care service. We tabulated underlying disease, HFNC F_{IO_2} and flows, breathing frequency, and oxygen saturation before and after HFNC, escalation to NIV, and hospital mortality for all subjects.

HFNC was delivered by the Fisher & Paykel Optiflow system, using the MR850 respiratory humidifier with MR290 chamber; RT241 heated delivery tubing, and RT033 or RT044 small or wide bore nasal cannulae (Fisher & Paykel Healthcare, Auckland, New Zealand). Therapy typically was initiated at previous F_{IO_2} and a flow of 35 L/min, titrating flow upward if tolerated to 45–50 L/min. F_{IO_2} was then titrated to maintain $S_{aO_2} > 90\%$, or according to specific clinical orders.

We included patients if they had DNR/DNI resuscitation status, clinical evidence of respiratory distress (dyspnea, tachypnea), hypoxemia, and mild or compensated hypercapnia ($P_{aCO_2} \leq 65$ and pH > 7.28). Patients were excluded if they were receiving comfort care only or if there was no intention to progress to NIV if indicated. The primary end point was the need for escalation to NIV, determined by the primary ICU service physicians. Secondary end points included clinical parameters of ventilation and gas exchange, and patient tolerance of HFNC. Mean changes in oxygen saturation and breathing frequency before and after HFNC were compared. Arterial blood gas data were available for all subjects at baseline. After HFNC, blood gases were variable in availability, timing, and relation to other clinical observations. Data were analyzed using the closest values prior to HFNC, and approximately 1 hour after starting HFNC, with subjects serving as their own controls. Statistical comparisons were evaluated by paired *t* test and the Wilcoxon signed-rank test.

QUICK LOOK

Current knowledge

Patients at the end of life and with do-not-intubate orders often receive noninvasive ventilation (NIV) to improve comfort and reduce breathlessness. High-flow, humidified oxygen via nasal cannula might provide similar symptom relief and thus obviate NIV.

What this paper contributes to our knowledge

High-flow, humidified nasal oxygen reduced hypoxemia in do-not-intubate patients and reduced the need for NIV.

Results

Fifty subjects with DNI status, 25 men and 25 women, received HFNC. Baseline characteristics are summarized in Table 1. Mean age was 73 years (range 27–96 years). Diagnoses, allowing multiple conditions, included pulmonary fibrosis (15), pneumonia (15), COPD (12), cancer (7), hematologic malignancy (7), congestive heart failure (3), pulmonary embolism (2), sepsis (2), alveolar hemorrhage (1), and myocardial infarction (1). Baseline arterial blood gases showed a mean P_{aO_2} of 66.5 mm Hg (range 39–121 mm Hg), a mean P_{aCO_2} of 42.3 mm Hg (range 26–65 mm Hg), and a mean pH of 7.42 (range 7.30–7.51). For the baseline arterial blood gases, in 29 subjects for whom F_{IO_2} (rather than liter flow) was specified, the median F_{IO_2} was 0.6 (range 0.21–1.0). For 21 remaining subjects on nasal cannula or mask, the median flow was 4 L/min (range 2–15 L/min). Blood gases were available in 23 subjects after HFNC, showing a mean P_{aO_2} of 95.4 mm Hg, a mean P_{aCO_2} of 40.2 mm Hg, and a mean pH of 7.43. There was no significant difference in the paired P_{aCO_2} measurements before and after HFNC (mean P_{aCO_2} 40.2 mm Hg to 39.9 mm Hg post-HFNC). Among those with post-HFNC blood gases, no subject showed a change of > 6 mm Hg in P_{aCO_2}.

Results are summarized in Table 2. HFNC was delivered at a mean F_{IO_2} of 0.67 (range 0.3–1.0) and a mean flow of 42.6 L/min (range 30–60 L/min). Breathing frequency decreased from 30.6 breaths/min to 24.7 breaths/min on HFNC ($P < .001$). Mean oxygen saturation improved from 89.1% to 94.7% ($P < .001$). Nine of the 50 (18%) of subjects escalated to NIV, while 41/50 (82%) were maintained on HFNC until improvement or withdrawal of support. Overall hospital mortality was 60% (30/50), ranging from 33.3% in the subjects with COPD and congestive heart failure, to 73.3% in the subjects with pulmonary fibrosis (see Table 1). Of the 9/50 (18%) who

Table 1. Subject Characteristics ($n = 50$)

Male	25
Female	25
Age, mean y	73
Age range, y	27–96
Diagnosis for hypoxemic respiratory failure, no. (hospital mortality %)	
Pulmonary fibrosis	15 (73.3)
Pneumonia	15 (46.7)
COPD	12 (33.3)
Congestive heart failure	3 (33.3)
Solid malignancy	7 (57)
Hematologic malignancy	7 (71.4)
Sepsis	2 (50)
Pulmonary embolism	2 (50)
Myocardial infarct	1 (0)
Hemorrhage	1 (100)

Table 2. Outcome of High-Flow Nasal Oxygen in 50 Subjects* With Do-Not-Intubate Status

	Pre-HFNC	Post-HFNC	*P*
Breathing frequency, breaths/min	30.6	24.7	< .001
O_2 saturation	89.1	94.7	< .001

* 41/50 (82%) were maintained on high-flow nasal cannula (HFNC). 9/50 (18%) escalated to noninvasive ventilation. Overall hospital mortality was 60%. The mean HFNC F_{IO_2} was 0.67 (range 0.3–1.0). The mean HFNC flow was 42.6 L/min (range 30–60 L/min).

progressed to NIV, 6 of 9 died (67%), versus death in 24 of 41 (58%) who did not receive NIV ($P = .72$). Of the 9 who went on to NIV, the majority (6/9) had underlying pulmonary fibrosis, 2 had COPD, and there was 1 with sepsis. Median duration of use of HFNC was 30 hours (mean 41.9 h, range 2–144 h). HFNC was well tolerated, with no episodes of nasal bleeding or facial skin breakdown.

Discussion

NIV can reverse hypoxemic respiratory distress in some DNR/DNI subjects, especially those with COPD and cardiogenic pulmonary edema.[9-11] However, many patients have difficulty tolerating a tight-fitting mask, and it has been urged that informed consent and the goals of therapy be clearly identified in this population.[12] We have observed that many DNI patients with hypoxemic respiratory failure are transferred or admitted to ICU specifically for a possible application of NIV. This not only taxes ICU resources but may not reflect the actual goals of therapy or the intent of the patient and surrogate decision makers.

Humidified HFNC oxygen therapy can provide comfortable delivery of high inspired O_2 concentration, and provides a small amount of PEEP, especially with the mouth closed.[5,6,13-15] Humidification may benefit mucociliary clearance, mobilization of respiratory secretions, and patient comfort.[16,17] HFNC may be as effective as and better tolerated than face mask techniques. Recent data suggest that HFNC may provide adequate support for patients hypoxemic from a variety of causes. In prospective, observational studies of patients with acute hypoxemic respiratory failure, mostly related to pneumonia, Sztrymf and colleagues found that HFNC improved oxygenation, breathing frequency, heart rate, dyspnea score, and use of accessory muscles of respiration.[18,19] In 20 subjects with acute hypoxemic respiratory failure, Roca and colleagues found that, compared to standard face mask oxygen, HFNC provided better oxygenation, dyspnea relief, and comfort.[20] Parke and colleagues randomized 60 postoperative cardiovascular surgery subjects with mild to moderate hypoxemia to HFNC or standard high-flow mask.[21] HFNC patients were more likely to succeed with the assigned therapy. In a series of hypoxemic cancer patients at Sloan-Kettering, including those with a DNR order, HFNC has been observed to provide adequate oxygenation and palliation, and to help avoid ICU admission.[22] They observed outcomes similar to our series, with 15% of patients declining while on HFNC, and overall mortality of 55%.

We observed that for subjects with hypoxemia and mild hypercapnia, use of HFNC was well tolerated and provided acceptable oxygenation without escalation to NIV in 82% of subjects. There was a relatively high fraction of subjects with end-stage pulmonary fibrosis, perhaps reflecting our referral practice and the exclusion of patients with severe hypercapnia. Our subjects were very ill, evidenced by 60% overall hospital mortality. HFNC appears to provide therapeutic and palliative benefit in this population. HFNC requires less training than NIV and may be more acceptable to hospital staff. This modality could be more broadly applied and might allow many patients to be treated outside the ICU environment.

Limitations of this study include the retrospective analysis of clinical data from a single institution. The mixture of diagnoses provides relatively small samples for generalization, such as a broader consideration for the COPD population. Patients with severe hypercapnia or acidosis were excluded. Baseline arterial blood gases and corresponding inspired oxygen concentrations varied in timing prior to ICU admission or transfer, and relative to the initiation of HFNC. Arterial blood gas data were not available for many subjects early after initiation of HFNC. As the subjects were DNR/DNI, variable levels of support were planned or delivered. Progression to NIV can be a subjective decision. The most common reasons cited in the records were continued oxygen desaturation, dyspnea, or tachypnea. The study was observational and we did not attempt to intervene in the therapy chosen by the primary

critical care service. Of note, however, despite the overall severity of illness, only 18% of subjects progressed to NIV. Since the subjects were all studied in the ICU, the hypothesis that similar patients could be managed on the general ward was not tested. This could be the basis of a prospective comparison of techniques for management of hypoxemic respiratory failure in this population.

Conclusions

Humidified HFNC oxygen therapy can provide adequate oxygenation for many patients with hypoxemic respiratory failure, and may be an alternative to NIV for patients who decline intubation.

REFERENCES

1. Antonelli M, Conti G, Esquinas A, Montini L, Maggiore SM, Bello G, et al. A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome. Crit Care Med 2007;35(1):18-25.
2. Garpestad E, Brennan J, Hill NS. Noninvasive ventilation for critical care. Chest 2007;132(2):711-720.
3. Garpestad E, Hill NS. Noninvasive ventilation for acute lung injury: how often should we try, how often should we fail? Crit Care 2006; 10(4):147.
4. Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: mechanisms of action. Respir Med 2009;103(10): 1400-1405.
5. Groves N, Tobin A. High flow nasal oxygen generates positive airway pressure in adult volunteers. Aust Crit Care 2007;20(4):126-131.
6. Parke R, McGuinness S, Eccleston M. Nasal high-flow therapy delivers low level positive airway pressure. Br J Anaesth 2009;103(6): 886-890.
7. Tiruvoipati R, Lewis D, Haji K, Botha J. High-flow nasal oxygen vs high-flow face mask: a randomized crossover trial in extubated patients. J Crit Care 2010;25(3):463-468.
8. Kacmarek RM. Should noninvasive ventilation be used with the do-not-intubate patient? Respir Care 2009;54(2):223-229.
9. Schettino G, Altobelli N, Kacmarek RM. Noninvasive positive pressure ventilation reverses acute respiratory failure in select "do-not-intubate" patients. Crit Care Med 2005;33(9):1976-1982.
10. Sinuff T, Cook DJ, Keenan SP, Burns KE, Adhikari NK, Rocker GM, et al. Noninvasive ventilation for acute respiratory failure near the end of life. Crit Care Med 2008;36(3):789-794.
11. Levy M Tanios MA, Nelson D, Short K, Senechia A, Vespia J, Hill NS. Outcomes of patients with do-not-intubate orders treated with noninvasive ventilation. Crit Care Med 2004;32(10):2002-2007.
12. Curtis JR Cook DJ, Sinuff T, White DB, Hill N, Keenan SP, et al. Noninvasive positive pressure ventilation in critical and palliative care settings: understanding the goals of therapy. Crit Care Med 2007;35(3):932-939.
13. Corley A, Caruana LR, Barnett AG, Tronstad O, Fraser JF. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. Br J Anaesth 2011;107(6):998-1004.
14. Parke RL, Eccleston ML, McGuinness SP. The effects of flow on airway pressure during nasal high-flow oxygen therapy. Respir Care 2011;56(8):1151-1155.
15. Ritchie JE, Williams AB, Gerard C, Hockey H. Evaluation of a humidified nasal high-flow oxygen system, using oxygraphy, capnography and measurement of upper airway pressures. Anaesth Intensive Care 2011;39(6):1103-1110.
16. Chanques G, Constantin JM, Sauter M, Jung B, Sebbane M, Verzilli D, et al. Discomfort associated with underhumidified high-flow oxygen therapy in critically ill patients. Intensive Care Med 2009; 35(6):996-1003.
17. Hasani A, Chapman TH, McCool D, Smith RE, Dilworth JP, Agnew JE. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. Chron Respir Dis 2008;5(2):81-86.
18. Sztrymf B, Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D, Ricard JD. Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intensive Care Med 2011;37(11):1780-1786.
19. Sztrymf B, Messika J, Mayot T, Lenglet H, Dreyfuss D, Ricard JD. Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: a prospective observational study. J Crit Care 2012;27(3):324. e9-e13.
20. Roca O, Riera J, Torres F, Mascians JR. High-flow oxygen therapy in acute respiratory failure. Respir Care 2010;55(4):408-413.
21. Parke RL, McGuinness SP, Eccleston ML. A preliminary randomized controlled trial to assess effectiveness of nasal high-flow oxygen in intensive care patients. Respir Care 2011;56(3):265-270.
22. Epstein AS, Hartridge-Lambert SK, Ramaker JS, Voigt LP, Portlock CS. Humidified high-flow nasal oxygen utilization in patients with cancer at Memorial Sloan-Kettering Cancer Center. J Pall Med 2011;14(7):835-839.