The Use of High-Flow Nasal Cannula Oxygen Outside the ICU

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BACKGROUND: High-flow nasal cannula (HFNC) oxygen therapy is a routine, evidence-based treatment in the ICU. Due to its ease of application, non–evidence-based use of HFNC has spread to non-ICU wards. This study reports on the experience with HFNC outside the ICU. METHODS: This is an observational study of HFNC prescribed by treating physicians in non-ICU areas. Primary outcomes included change in dyspnea visual analog scale score and physiological variables both before and 30 min after initiation of HFNC treatment. Secondary outcomes included mortality, ICU admission, and intubation. RESULTS: We observed decreased median (interquartile range) visual analog scale scores after initiation of HFNC: 8 (6–9) versus 5 (4–6) ($P < .001$) in 90 of 111 subjects (81%, 95% CI 72.5–87.9%, $P < .001$). Breathing frequency (31 ± 10 vs 26 ± 7 breaths/min, $P < .001$) and saturation (84 ± 12% vs 94 ± 5%, $P < .001$) also improved. Overall cohort mortality was 55 of 111 subjects (50%); however, 41 of 111 subjects (33%) had a do not resuscitate (DNR) order. Among 70 non-DNR subjects, early mortality (< 72 h) occurred in 9 of 70 subjects (13%), and late mortality in 12 of 70 subjects (17%). The composite end point (ie, discharged alive, non-intubated, not admitted to ICU) was met by 35 of 70 subjects (50%) without a DNR order. An increased ROX index ($[S_{pO_2}/F_{IO_2}]$/breathing frequency) was the only independent predictor associated with achieving the composite outcome (odds ratio 1.51, 95% CI 1.1–2.0, $P = .01$). Higher pre-connection visual analog scale score (odds ratio 1.75, 95% CI 1.35–2.28, $P < .001$) and a history of respiratory disease (odds ratio 3.52, 95% CI 1.27–9.72, $P = .01$) were predictors of greater improvement in dyspnea with HFNC. No variable predicted mortality. CONCLUSIONS: HFNC outside the ICU was associated with improved visual analog scale score, breathing frequency, and saturation but with a relatively high mortality, even in non-DNR subjects. HFNC was used in many subjects who had a DNR order. This therapy may have been palliative in intent. Care should be exercised in using this therapy in a setting that is not continuously monitored. *Key words: HFNC; respiratory failure; medical ward; ICU; non invasive ventilation; outcome; oxygen therapy.* [Respir Care 2019;64(11):1333–1342. © 2019 Daedalus Enterprises]

Introduction

High-flow nasal cannula (HFNC) oxygen therapy has an increasing role as an effective noninvasive therapy for patients with respiratory failure in ICUs.[1-5] The technology is based on flow of up to 60 L/min of an air/oxygen mixture through a heater/humidifier to a wide-bore nasal cannula. The high flow generates low PEEP and decreases dead space.[6] In contrast to noninvasive ventilation delivered through a mask, there is limited support of carbon dioxide elimination,[7] however the nasal cannula is much more comfortable than a tightly applied face mask.[8,9]

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HFNC therapy has been shown to be superior to traditional oxygenation support tools (eg, low-flow nasal cannula, face mask) in improving respiratory indices such as breathing frequency, oxygen saturation, and dyspnea[10] and compares well to noninvasive mask ventilation in certain circumstances.[1,11,12] These findings are supported by meta-analyses[13] but are not universal.[14-16]

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The ease of use, apparent lack of complications, and success in therapy have led to the use of HFNC beyond the ICU. However, use of HFNC in other settings is not based on evidence and has not been widely evaluated. In this study we examine use of HFNC outside the ICU to identify the patients chosen, effectiveness of therapy, and patient outcomes.

QUICK LOOK

Current knowledge

The use of high-flow nasal cannula (HFNC) to deliver oxygen therapy has been investigated mainly in monitored environments such as ICUs, emergency departments, and post-anesthesia care units. HFNC has been reported to improve patient comfort and physiological measures, and to be associated with minimal complications.

What this paper contributes to our knowledge

The application of HFNC oxygen to subjects with continued hypoxemia despite oxygen therapy by traditional means in minimally monitored beds in medical and geriatric wards was associated with improved visual analog scale scores and physiological measures in all subgroups examined. HFNC use was associated with high mortality, particularly in subjects with a do not resuscitate order. Among other subjects, mortality was similar to expected.

Methods

We performed a prospective observational study of subjective and objective measures of dyspnea obtained before and after administration of HFNC to patients with hypoxemic respiratory failure outside the ICU. The study included consecutive adult subjects for whom treating physicians decided to administer HFNC in the medical division (including general medical, intermediate medical units, geriatrics, and hemato-oncology wards) as well as the emergency department of the Shaare Zedek Medical Center, a 750-bed academic tertiary referral center in Jerusalem, Israel. The hospital ethics committee waived the requirement for informed consent (0104-15-SZMC) because the study was observational. The decision to administer HFNC was not part of the study protocol, being at the sole discretion of the treating physicians. Vital signs were collected as part of routine clinical care, and additional subject participation was limited to providing a subjective measure of dyspnea before and after administration of HFNC via the visual analog scale score for dyspnea. Patients under 18 y old, pregnant women, patients with tracheostomy, or patients who had received prior treatment with HFNC were excluded.

Subjective and objective measures were recorded immediately prior to administration of HFNC and 30 min later by the respiratory therapist applying the therapy. The subjective measure of dyspnea was evaluated using a visual analog scale score as an ordinal scale. Subjects were asked to describe the degree of their shortness of breath and assign a value ranging from 0 (no distress) to 10 (worst distress possible). While this is not a true visual analog scale measurement of symptom severity, we used this term for simplicity. Objective physiological variables included pulse, blood pressure, breathing frequency, and oxygen saturation measured using pulse oximetry. Demographic, medical, and outcome data were obtained from the medical record.

Data Analysis

The primary outcome measures of effectiveness were changes in visual analog scale score, pulse, blood pressure, breathing frequency, and oxygen saturation after initiation of treatment. Secondary outcomes included mortality, ICU admission, and intubation. A composite outcome measure of treatment success was defined as subjects who survived to hospital discharge, were not admitted to ICU, and were not intubated. The ROX index ($[S_{pO_2}/F_{IO_2}]$/breathing frequency) at 30 min after administration of HFNC oxygen was calculated for subjects meeting or failing the composite outcome measure.[17,18]

Subgroup Analysis

Survivors were compared to non-survivors after exclusion of subjects with a do not resuscitate (DNR) order to identify risk factors for mortality. Mortality was divided into early mortality ($\leq$ 72 h after application of HFNC), and late mortality ($>$ 72 h after application of HFNC). The term "DNR order" is used as a generic term to include all orders to limit initiation of therapies including intubation and cardiopulmonary resuscitation. Outcomes were also compared for subjects with and without a DNR order.

Subjects who reported improved visual analog scale scores were compared to those without improvement in an attempt to identify factors associated with benefit from HFNC therapy. The median improvement in visual analog scale score was identified from the whole study population. The population was then divided into 2 groups: those with a decrease in visual analog scale score that was greater than the median change (improved Δ visual analog scale group), and those with a change in visual analog scale less than or equal to the median change (unimproved Δ visual analog scale group). Therapy and subject outcomes were also compared according to the composite outcome measure (ie, no intubation, no ICU admission, and hospital discharge alive).

Sample size was estimated from prospective preliminary data. Assuming 90% of subjects reported improved visual analog scale scores, as was reported in an unpublished preliminary study, a power analysis (using Fisher exact test) calculated that a sample of 120 subjects would be sufficient to demonstrate improved dyspnea (95% CI 83.2–94.7%).

Changes in visual analog scale were analyzed with the Wilcoxon test. Changes in physiological measures per subject were analyzed using the paired *t* test. Differences between group means were compared using the *t* test. Qualitative variables were compared using the chi-square test or Fisher exact test. Multivariate logistic regression was used to identify predictors of improvement in visual analog scale scores. The population was divided into 2 groups (ie, improved visual analog scale vs unimproved visual analog scale), and variables present prior to connection, which were measured for > 10 subjects and associated with improvement at $P < .1$ (pre-connection visual analog scale score and past medical history of respiratory failure) were included as explanatory variables. Logistic regression was also used to identity independent predictors of the composite outcome measure in non-DNR subjects including age, ROX index, Δ visual analog scale, and length of stay prior to starting HFNC therapy as predictor variables. Multiple collinearity was investigated using a correlation matrix, tolerance, variance inflation, and colinearity index. No collinearity was identified in either analysis. All analyses were performed using SAS 9.2 (SAS Institutes, Cary, North Carolina); all tests were 2-tailed, and significance was defined as $P < .05$.

Results

Data were collected on 176 HFNC administrations from December 2015 to December 2017. Exclusion criteria were present on 7 occasions, and visual analog scale scores were not adequately recorded on 58 occasions, leaving 111 events for analysis. Mean length of stay prior to HFNC therapy was 7 ± 10 d, and mean duration of therapy was 93 ± 124 h.

Primary Outcomes

After initiation of HFNC treatment, 90 of 111 subjects (81%, 95% CI 72.5–87.9%, $P < .001$) reported improved dyspnea with decreased visual analog scale scores: pre-HFNC median (interquartile range [IQR]) visual analog scale score was 8 (6–9) vs median (IQR) post-HFNC score of 5 (4–6), $P < .001$. Visual analog scale scores decreased significantly in most etiology subgroups. In parallel, pulse and breathing frequency decreased significantly, and oxygen saturation significantly increased (Table 1).

Secondary Outcomes

Of the 111 subjects treated with HFNC, 55 (50%) died, 24 (22%) within 72 h of beginning HFNC (ie, early mortality) and 31 (28%) later (ie, late mortality). However, 41 of 111 (33%) subjects in the cohort had a DNR order, of whom 38 of 41 (93%) died. Among the 70 subjects without a declared DNR order, overall mortality was 18 of 70 (26%): early mortality for 9 of 70 (13%); late mortality for 9 of 70 (13%). The mean time from starting HFNC to death was 7.2 ± 8.6 d. Mortality ranged from 8 of 46 (17%) in the internal medicine ward to 5 of 11 (45%) in the hemato-oncology ward.

Among subjects without a DNR order, 13 of 70 (19%) subjects were admitted to ICU (9 subjects ≤ 72 h, and 4 subjects > 72 h after beginning HFNC; mean time from starting HFNC to ICU admission was 2.1 ± 2.9 d), and 18 of 70 (26%) subjects were intubated (12 subjects ≤ 72 h, and 6 subjects > 72 h, with a mean time to intubation of 4.2 ± 7.6 d).

Subgroup Analyses

Composite Outcome Measure. Overall, 35 of 70 (50%) subjects without a DNR order met the composite outcome measure for successful treatment (ie, no ICU admission, no intubation, and survival to hospital discharge) (Table 2). Among these subjects, the ROX index was calculated as S_{pO_2}/F_{IO_2}/breathing frequency. The ROX index has been used to predict the success of HFNC therapy, with a higher score indicating a higher probability of successful therapy.[17,18] The score was 8.2 ± 3.6 for subjects with successful therapy versus 5.1 ± 1.9, $P < .001$ for subjects with unsuccessful therapy (ie, subject was admitted to ICU, was intubated, or died during admission). Multivariate analysis, with time from admission to HFNC, change in visual analog scale score, ROX index, and age as predictor variables, showed that only increasing ROX index was asso-

Table 1. Visual Analog Scale Scores for Dyspnea and Physiological Variables Before and After HFNC Therapy

	n	Before HFNC Therapy	After HFNC Therapy	Mean Difference (paired data)	*P*
Visual Analog Scale Scores					
Whole population	111	8 (6–9)	5 (4–6)	−2 (−4 to −1)	< .001
By hypoxia etiology*					
Pneumonia	66	7.5 (6–8.5)	5 (4–6)	−2 (−4 to −1)	< .001
Sepsis	25	8 (6–10)	5 (4–6)	−2 (−4 to −1)	< .001
Congestive heart failure	25	8 (6–8)	4 (4–6)	−2 (−5 to −1)	< .001
Malignancy	18	8 (6–9)	6 (4–6)	−2 (−4 to 0)	< .001
Restrictive lung disease	8	6.5 (5.5–9)	4 (2–5.5)	−3.5 (−6 to −1)	.031
COPD	5	10 (8–10)	2 (2–5)	−5 (−6 to −4)	.062
Physiological Variables					
Pulse, beats/min		97.4 ± 22.5	93.2 ± 19.6	−4.6 ± 13.7	.002
Blood pressure, mm Hg					
Systolic		120.0 ± 26.2	117.6 ± 22.8	−2.5 ± 17.1	.18
Diastolic		68.1 ± 15.3	67.2 ± 12.5	−0.5 ± 14.0	.75
Oxygen saturation, %		84.1 ± 12.3	93.7 ± 4.9	9.4 ± 11.2	< .001
Breathing frequency, breaths/min		30.6 ± 9.7	25.8 ± 7.2	−5.6 ± 7.1	.001

Visual analog scale scores presented as median (interquartile range). Physiological data are presented as mean ± SD. Change data represent mean of paired change.
* Overlap exists between etiologies.
HFNC = high-flow nasal cannula

ciated with improved probability of successful therapy (odds ratio [OR] 1.51, 95% CI 1.10–2.07, $P = .01$).

Mortality. None of the demographic, etiological, or physiological variables recorded were associated with survival status in subjects without a DNR order (Table 3).

Improved Visual Analog Scale. The median difference between visual analog scale scores before and after initiation of treatment (Δ visual analog scale) was −2 (Table 4). Multivariate analysis using visual analog scale score prior to HFNC administration and past medical history of respiratory disease as predictor variables indicated that both of these variables were predictors of improved visual analog scale (pre-HFNC administration visual analog scale score: OR 1.75, 95% CI 1.35–2.28, $P < .001$; past history of respiratory disease OR 3.52, 95% CI 1.27–9.72, $P = .01$).

Subjects With a DNR Order. Visual analog scale scores improved similarly for subjects with DNR orders and subjects without DNR orders: median change (IQR) in visual analog scale scores subjects with vs without a DNR order was −2 (−3.5 to −1.0) versus −2 (−4 to −1), $P = .49$ (Table 5).

Missing Data

A comparison of basic demographics and outcomes for subjects for whom data were not collected with the 111 subjects with adequate study data revealed similar results (age 70 ± 19 vs 75 ± 17 y, $P = .14$; male sex 55% vs 50%, $P = .57$; and overall mortality 50% vs 44%, $P = .35$).

Discussion

The use of HFNC outside the ICU is effective, in that its use is associated with a decrease in the severity of dyspnea in the large majority of subjects (81%) and improved physiological parameters. Further, 50% of the non-DNR subjects included in the cohort met the composite success outcome measure of no intubation, no ICU admission, and survival to hospital discharge. The safety of the therapy was initially of significant concern in view of the high overall mortality (50%). However, it was discovered that a large proportion (33%) of the cohort were subject to DNR orders, and that early mortality (< 72 h after commencing therapy) among non-DNR subjects was considerably lower (13%), which was somewhat reassuring. No pretreatment parameters were significant predictors of mortality, although worse dyspnea (as measured by a higher pre-administration visual analog scale score) and the presence of preexisting respiratory disease were both significant predictors of efficacy (as measured by a decrease in visual analog scale of dyspnea). Immediate physiological improvement (improved ROX index at 30 min) was a significant predictor of good outcome (achievement of the composite outcome measure - no ICU admission, no intubation and survival to hospital discharge).

Very few studies have been performed on HFNC outside of the ICU. A study on subjects with cardiogenic

Table 2. Comparison of Subjects Grouped by Composite Outcome Measure Among Non-DNR Subjects

	Composite Success	Composite Failed	*P*	Multivariate Analysis	
				Odds Ratio (95% CI)	*P*
Subjects, *n* (%)	35 (50)	35 (50)			
Male sex, *n* (%)	19 (54)	14 (40)	.23		
Age, y	77 ± 17	70 ± 15	.10	1.02 (0.97–1.07)	.42
Medical Background*					
Cardiovascular	20 (57)	19 (54)	.81		
Respiratory	5 (14)	10 (29)	.14		
Hypertension	22 (63)	20 (57)	.63		
Diabetes mellitus	14 (40)	12 (34)	.62		
Malignancy	5 (14)	5 (14)	.99		
Active smoker	5 (14)	6 (17)	.74		
CO_2 retention per history	23 (68)	21 (64)	.73		
Etiology of Respiratory Failure*					
Pneumonia	21 (60)	24 (69)	.45		
Congestive heart failure	6 (17)	9 (26)	.38		
Malignancy	3 (9)	2 (6)	.64		
Sepsis	10 (29)	6 (17)	.25		
COPD	2 (6)	3 (9)	.64		
Other lung disease	2 (6)	2 (6)	.99		
Vital Signs and Physical Data					
Fever	24 (69)	27 (79)	.30		
Bacteremia	4 (12)	3 (10)	.94		
Pulse before HFNC	91 ± 22	99 ± 21	.18		
Systolic before HFNC	118 ± 23	115 ± 29	.65		
Diastolic before HFNC	68 ± 12	65 ± 16	.38		
Breathing frequency before HFNC	28 ± 10	31 ± 10	.43		
S_{pO_2} before HFNC	87 ± 8	83 ± 11	.09		
Visual analog scale before HFNC	7 (5–9)	8 (6–9)	.67		
Δ Pulse	−5 ± 11	−2 ± 15	.46		
Δ Systolic blood pressure	0 ± 13	2.4 ± 18	.56		
Δ Diastolic blood pressure	−1 ± 11	2 ± 19	.61		
Δ Breathing frequency	−6 ± 8	−5 ± 7	.59		
Δ Oxygen saturation	8 ± 8	9 ± 9	.67		
Δ Visual analog scale	−4 (−5 to −2)	−2 (−3 to 0)	.003	0.84 (0.62–1.15)	.27
ROX Index	8.2 ± 3.6	5.1 ± 1.9	< .001	1.51 (1.10–2.07)	.01
Treatment and Hospitalization					
Initial F_{IO_2}	0.68 ± 0.22	0.79 ± 0.19	.02		
Initial gas flow, L/min	45 ± 8	47 ± 9	.19		
Duration of HFNC, h	95 ± 92	67 ± 129	.30		
Length of stay, d	18 ± 10	34 ± 42	.046		
Admission to HFNC, d	5 ± 6	8 ± 9	.08	0.94 (0.84–1.05)	.29
HFNC to discharge, d	13 ± 7	26 ± 41	.10		

The composite outcome measure for successful therapy included no intubation, no ICU admission, and hospital discharge alive. Data are presented as mean ± SD, frequency (%), or median (interquartile range).

* Overlap exists between etiologies.

DNR = do not resuscitate order

HFNC = high-flow nasal cannula

Δ = difference between first and second measurement

ROX = ratio of S_{pO_2}/F_{IO_2} to breathing frequency

pulmonary edema in the emergency department showed significant improvements in breathing frequency using HFNC compared to conventional oxygen therapy (with a decrease in breathing frequency from 28.7–21.8 breaths/min for HFNC and 28.6–25.1 breaths/min for conventional oxygen therapy).[19] However, there were no significant changes in the

Table 3. Mortality Analysis Amongst Non-DNR Subjects

	Alive	Died	*P*
Subjects, *n* (%)	52 (74)	18 (26)	
Male sex, *n* (%)	23 (44)	10 (19)	.40
Age, y	73 ± 17	74 ± 14	.88
Medical Background*			
Cardiovascular	28 (54)	11 (21)	.59
Respiratory	10 (19)	5 (10)	.51
Hypertension	28 (54)	14 (27)	.07
Diabetes mellitus	18 (35)	8 (15)	.45
Malignancy	6 (12)	4 (8)	.26
Active smoker	8 (15)	3 (6)	> .99
Etiology of Respiratory Failure*			
Pneumonia	33 (63)	12 (23)	.80
Congestive heart failure	13 (25)	2 (4)	.32
Malignancy	2 (4)	3 (6)	.10
Sepsis	11 (21)	5 (10)	.53
COPD	3 (6)	2 (4)	.59
Other lung disease	3 (6)	1 (2)	> .99
Vital Signs and Physical Data			
CO_2 retention	17 (33)	6 (12)	.91
Fever	13 (25)	5 (10)	> .99
Bacteremia	4 (8)	3 (6)	.24
Pulse before HFNC	94 ± 22	96 ± 22	.75
Systolic before HFNC	117 ± 25	117 ± 30	.97
Diastolic before HFNC	67 ± 13	66 ± 18	.82
Breathing frequency before HFNC	29 ± 11	31 ± 5	.29
S_{pO_2} before HFNC	88 ± 9	83 ± 12	.29
Visual analog scale before HFNC	7 (5.5–9)	8 (6–10)	.25
Δ Pulse	−4 ± 13	−3 ± 14	.71
Δ Systolic blood pressure	1 ± 16	1 ± 14	.90
Δ Diastolic blood pressure	−0.6 ± 16	4 ± 13	.36
Δ Breathing frequency	−7 ± 8	−2 ± 6	.067
Δ Oxygen saturation	9 ± 9	9 ± 9	.94
Δ Visual analog scale	−2.5 (−4.5 to −1)	−2 (−3 to 0)	.45
Treatment and Hospitalization			
Initial F_{IO_2}	0.72 ± 0.22	0.80 ± 0.19	.16
Initial gas flow, L/min	46 ± 8	48 ± 9	.35
Duration of treatment, h	87 ± 110	62 ± 118	.42
Length of stay, d	29 ± 36	17 ± 14	.045
Time from admission to treatment, d	5 ± 6	10 ± 10	.09
Treatment to discharge/death	24 ± 34	7 ± 8	.002

This is a comparison of demographic, physiologic, and treatment parameters according to survival status for the 70 subjects without a do not resuscitate order. Data are presented as mean ± SD, frequency (%), or median (interquartile range).
* Overlap exists between etiologies.
HFNC = high-flow nasal cannula
Δ = difference between first and second measurement

admission rate, length of stay in the emergency department and hospital, use of noninvasive ventilation, intubation, or mortality. In a non-ICU study in 67 subjects, similar clinical improvements were achieved for 68.7% of subjects, with low mortality (7.5%) and ICU admission (4.5%).[20] This study demonstrated that administration of HFNC to subjects outside the ICU with hypoxemia/dyspnea led to improved breathing frequency and heart rate, as well as improved oxygen saturation. However, in contrast to our study, end-of-life patients, patients with a contraindication to positive-pressure ventilation, and patients in high-dependence units were excluded.[20] Our study included subjects meeting all of these criteria, which may explain the poorer outcomes. Indeed, one of the interesting findings in our study was the widespread

Table 4. Comparison of Subjects Grouped by Improved Visual Analog Scale Score

	Unimproved Visual Analog Scale Score	Improved Visual Analog Scale Score	*P*	Multivariate Analysis	
				Odds Ratio (95% CI)	*P*
Subjects, *n* (%)	62 (56)	49 (44)			
Male sex, *n* (%)	30 (48)	25 (51)	.78		
Age, y	73 ± 15	77 ± 18	.24		
Medical Background*					
Cardiovascular	33 (53)	32 (65)	.19		
Respiratory	12 (19)	18 (36)	.041	3.52 (1.27–9.72)	.01
Hypertension	36 (58)	31 (63)	.50		
Diabetes mellitus	26 (41)	15 (30)	.21		
Malignancy	11 (17)	10 (20)	.72		
Active smoker	7 (11)	9 (18)	.29		
Do not resuscitate order	25 (40)	16 (32)	.4		
Etiology of Respiratory Failure*					
Pneumonia	37 (59)	29 (59)	.95		
Congestive heart failure	13 (20)	12 (24)	.65		
Malignancy	11 (17)	7 (14)	.62		
Sepsis	15 (24)	10 (20)	.63		
COPD	0 (0)	5 (10)	.01		
Other lung disease	4 (6)	4 (8)	.73		
Vital Signs and Physical Data					
CO_2 retention	18 (29)	17 (34)	.35		
Fever	18 (29)	9 (19)	.21		
Bacteremia	7 (11)	2 (4)	.17		
Pulse before HFNC	99 ± 22	96 ± 24	.56		
Systolic before HFNC	118 ± 28	122 ± 24	.45		
Diastolic before HFNC	67 ± 17	69 ± 13	.62		
Breathing frequency before HFNC	29 ± 8	32 ± 11	.22		
S_{pO_2} before HFNC	85 ± 10	82 ± 14	.24		
Visual analog scale before	6.5 (6–8)	8.0 (8–9)	< .001	1.75 (1.35–2.28)	< .001
Δ Pulse	−3 ± 13	−7 ± 14	.09		
Δ Systolic blood pressure	−5 ± 17	1 ± 16	.07		
Δ Diastolic blood pressure	−1 ± 16	0 ± 12	.76		
Δ Breathing frequency	−3 ± 5	−7 ± 8	.030		
Δ Oxygen saturation	7 ± 8	12 ± 14	.01		
Δ Visual analog scale	−1 ± 1	−5 ± 1	< .01		
Treatment and Hospitalization					
Initial F_{IO_2}	0.78 ± 0.21	0.74 ± 0.20	.26		
Initial gas flow, L/min	45 ± 10	47 ± 9	.19		
Duration of HFNC, h	81 ± 116	100 ± 122	.41		
Length of stay, d	25 ± 16	20 ± 15	.41		
Admission to HFNC, d	7 ± 10	7 ± 10	.85		
HFNC to discharge, d	17 ± 32	13 ± 11	.35		

Data are presented as mean ± SD, frequency (%), or median (interquartile range).
* Overlap exists between etiologies.
HFNC = high-flow nasal cannula
Δ = difference between first and second measurement

use of HFNC among DNR subjects. In this population, HFNC was found to be equally effective at reducing dyspnea compared to the non-DNR population. Shortness of breath and respiratory difficulties are major and distressing symptoms at the end of life,[21-24] and HFNC may have a significant role in alleviating suffering,[22,23] possibly with an opiate-sparing effect.[24]

When treating hypoxemic respiratory failure with modalities other than intubation and invasive mechanical ventilation, there is a safety issue that needs to be ad-

Table 5. Comparison of Subjects Grouped by DNR Order Status

	DNR Order	No DNR Order	*P*
Subjects, *n* (%)	41 (37)	70 (63)	
Male sex, *n* (%)	22 (54)	33 (47)	.51
Age, y	76 ± 18	74 ± 16	.45
Medical Background*			
Cardiovascular	23 (56)	39 (56)	.43
Respiratory	15 (37)	15 (21)	.08
Hypertension	25 (61)	42 (60)	.92
Diabetes mellitus	15 (37)	26 (37)	.95
Malignancy	11 (27)	10 (14)	.10
Active smoker	5 (12)	11 (16)	.61
CO_2 retention	12 (32)	23 (34)	.84
Etiology of Respiratory Failure*			
Pneumonia	21 (51)	45 (64)	.18
Congestive heart failure	10 (24)	15 (21)	.72
Malignancy	13 (32)	5 (7)	< .001
Sepsis	9 (22)	16 (23)	.91
COPD	0 (0)	5 (7)	.15
Other lung disease	4 (10)	4 (6)	.46
Vital Signs and Physical Data			
Fever	9 (22)	18 (26)	.63
Bacteremia	2 (6)	7 (11)	.66
Pulse before HFNC	102 ± 23	95 ± 22	.13
Systolic before HFNC	125 ± 26	117 ± 26	.14
Diastolic before HFNC	70 ± 17	67 ± 14	.27
Breathing frequency before HFNC	33 ± 9	29 ± 10	.19
S_{pO_2} before HFNC	82 ± 15	85 ± 10	.29
Visual analog scale before HFNC	8 (6–9)	8 (6–9)	.36
Δ Pulse	−6 ± 15	−4 ± 13	.50
Δ Systolic blood pressure	−9 ± 18	1 ± 15	.01
Δ Diastolic blood pressure	−2 ± 11	0 ± 15	.44
Δ Breathing frequency	−6 ± 6	−6 ± 8	.92
Δ Oxygen saturation	10 ± 14	9 ± 9	.52
Δ Visual analog scale	−2 (−3.5 to −1.0)	−2 (−4 to −1)	.49
Treatment and Hospitalization			
Initial F_{IO_2}	0.80 ± 0.21	0.74 ± 0.21	.11
Initial gas flow, L/min	45 ± 9	46 ± 8	.74
Duration of HFNC, h	104 ± 128	81 ± 112	.33
Length of stay, d	18 ± 19	26 ± 32	.10
Admission to HFNC, d	9 ± 14	6 ± 7	.33
HFNC to discharge, d	9 ± 9	20 ± 30	.01

Data are presented as mean ± SD, frequency (%), or median (interquartile range).
* Overlap exists between etiologies.
DNR = do not resuscitate order
HFNC = high-flow nasal cannula
Δ = difference between first and second measurement

dressed. Numerous studies have demonstrated that delaying intubation in patients who are not doing well on noninvasive methods of oxygenation (eg, noninvasive ventilation or HFNC) may lead to worse outcomes.[1,25,26] Administering HFNC outside the ICU with minimal monitoring may delay timely airway intervention and intubation. However, we did not find a difference between the mortality of non-DNR subjects in this study and the mortality in other similar population cohorts.[27]

Our study has several limitations. Because this was an observational study, there was no control group for outcome comparison, although overall reported mortality for internal medicine department admissions is similar; eg, among 10,788 hospitalized patients in a 3.5-y period, 874 (8.1%)

died during their admission.[27] Study forms were completed for only 111 subjects out of the 176 subjects treated with HFNC, which could suggest a bias. This difference is most likely due to the fact that data collection was not performed reliably on weekends. Comparison of basic demographics between included subjects and subjects with inclusion criteria who were not part of the final analysis revealed that the populations were similar. Another limitation is that the number of analyzed subjects (ie, 111) did not reach the predetermined sample size of 120 subjects. However, even if 9 additional subjects were included and reported no benefit from therapy, the result would remain statistically significant because 90 of the 120 subjects would have reported improvement (75%), 95% CI 66–82, $P < .001$). Another limitation is that HFNC use was not protocolized, and many subjects received flows below the maximal flow of 60 L/min. HFNC parameters were set at the bedside by the respiratory therapist according to the clinical condition and the comfort of the subject. Further, gas flow was not a predictor of success in any of the analyses. Finally, the visual analog scale and physiological follow-up were limited to the observations immediately prior to and 30 min after administration of HFNC.

Conclusion

The use of HFNC therapy in the ward setting was effective, being associated with significantly improved comfort and physiological parameters. Overall mortality in non-DNR subjects was similar to that reported by others for similar hospital admissions. In addition, the therapy was used widely and effectively in DNR subjects, for whom there may be a beneficial palliative effect.

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