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SPECIFIC PATIENT POPULATION

MECHANISMS OF ACTION

Corley A, Caruana L, Barnett A, Tronstad O, Fraser J.
Br J Anaesth. 2011;107(6):998-1004.

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Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients.

AIM:

To assess the effects of high-flow oxygen therapy (HFOT) using high-flow nasal cannulae (HFNCs) compared with low-flow oxygen therapy on airway pressure (Paw) and end-expiratory lung volume (EELV). To identify a relationship, if any, between peak airway pressure and EELV.

METHOD:

In this prospective, non-randomised, interventional study, adult patients requiring HFOT after cardiac surgery (n=20) had a local anaesthetic nasal spray and nasal feeding tube fitted while sitting upright. Paw was measured using a precision pressure transducer [PPT-001, DWWW2V, Honeywell International Ltd] that was attached to the feeding tube. Changes in EELV were assessed indirectly via measurement of end-expiratory lung impedance (EELI) using an electrical impedance tomography (EIT) kit [EIT Evaluation Kit 2, Dräger Medical].

Air pressure and lung volume 2 min readings were taken simultaneously, first during low-flow oxygen therapy (face mask [FM] oxygen or nasal oxygen cannula) and then, following a 15 min washout period, during HFOT with the Optiflow™ system (MR850 heated and humidified, RT202 delivery tubing and RT050/051 nasal cannulae) [Fisher & Paykel Healthcare]. The Optiflow™ humidifier temperature was set to 37 °C and the fraction of inspired oxygen (FiO_2) titrated on an individual basis to maintain blood oxygen saturation (measured via pulse oximetry [SpO_2]) of ≥95%, with the flow rate initiated at 35 L/min and uptitrated to a maximum of 50 L/min. Measurements were taken with the patient's mouth both open and closed.

FiO_2 was also estimated during low-flow oxygen therapy. Other variables included respiratory rate, tidal impedance variation (VARt), oxygenation (ratio of partial pressure of arterial oxygen [PaO_2] to FiO_2) and subjective rating of dyspnoea (modified Borg score).

RESULTS:

HFOT with HFNC significantly increased mean Paw, EELI, VARt and oxygenation compared with low-flow oxygen therapy (table). The respiratory rate was lowered significantly with HFOT, and there was a trend to improved subjective dyspnoea.

There was a strong positive correlation between Paw and EELI (correlation coefficient=0.7; p<0.001). The mean percentage increase in EELI with HFOT as compared with low-flow oxygen therapy was greater in patients with a higher body mass index (BMI) [13.3% in those with BMI of 25 kg/m^2 versus 24.4% in thus with BMI of 40 kg/m^2].

VARIABLE	LOW-FLOW OXYGEN	HFOT WITH HFNC	DIFFERENCE		P VALUE
	Mean (SD)	Mean (SD)	Mean (SD)	95% CI	
EELI (units)	419 (212.5)	1936 (212.9)	1517 (46.6)	1425, 1608	<0.001
Paw (cm H_2O)	-0.3 (0.9)	2.7 (1.2)	3.0 (1.3)	2.4,3.7	<0.001
Respiratory rate (beats/min)	20.9 (4.4)	17.5 (4.6)	-3.4 (2.8)	−2.0, −4.7	<0.001
Borg score 0–10	2.7 (2.6)	1.9 (2.3)	-0.8 (1.2)	−0.1, −1.4	0.023
Tidal variation (units)	1512 (195.0)	1671 (195.1)	159 (21.6)	117, 201	<0.001
PaO_2/FiO_2 (mm Hg)	160 (53.7)	190.6 (57.9)	30.6 (25.9)	17.9, 43.3	<0.001

95% CI = 95% confidence interval; EELI = end-expiratory lung impedance; FiO_2 = fraction of inspired oxygen; HFOT = high-flow oxygen therapy; HFNC = high-flow nasal cannula; PaO_2 = partial pressure of arterial oxygen; Paw = airway pressure; SD = standard deviation.

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DISCUSSION:

Pulmonary complications after cardiac surgery are common. HFNCs are used to deliver high-flow humidified air and oxygen via wide-bored nasal cannulae at a set FiO_2. This is the first study to show that HFOT delivered by HFNC after cardiac surgery increases EELI in adults, suggesting increased lung volumes and functional residual capacity. Furthermore, increases in EELI were significantly influenced by BMI, suggesting that patients with a higher BMI may benefit from HFNC-induced low-level positive P_{aw} and increases in lung volume.

HFNC use also increased P_{aw} by 3.0 cm over that achieved with low-flow oxygen therapy. This increase was correlated with the increase in EELI. Positive airway pressure then improves lung volume, and concomitantly improves respiratory rate, subjective dyspnoea and oxygenation.

Further research is required to confirm these study results because gas flow rates were not standardized across patients, and the sample size was small.

CONCLUSION:

HFOT with HFNCs provides a modest increase in oropharyngeal P_{aw} that appears to result in clinically significant increases in EELV as compared with low-flow oxygen therapy. Patients experiencing respiratory dysfunction after cardiac surgery, particularly those with a high BMI or who cannot tolerate non-invasive ventilation, may benefit from HFNC.

KEY POINTS:

- HFNCs increase airway pressure as compared with low-flow oxygen therapy, and this increase is significantly correlated with increases in EELV.
- Lung tidal volume, respiratory rate, subjective dyspnoea and oxygenation were also improved after HFOT versus low-flow oxygen therapy.
- Benefits of HFOT were greatest in patients with a higher BMI.

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Lenglet H, Sztrymf B, Leroy C, Brun P, Dreyfuss D, Ricard J.
Respir Care. 2012;57(11):1873-1878.

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Humidified high flow nasal oxygen during respiratory failure in the emergency department: feasibility and efficacy.

AIM:

To determine the feasibility and effect of high flow nasal cannula (HFNC) in the treatment of patients with acute respiratory failure presenting to the emergency department (ED).

METHOD:

This was a prospective, observational study conducted in the ED of a university hospital in France on adult patients between January and April 2009. Patients being treated with a non-rebreathing high fraction of inspired oxygen (FiO_2) face mask with reservoir (Hudson RCI™, Teleflex Medical) were screened for study inclusion.

Patients were included in the study if dyspnea persisted despite being given aggressive conventional oxygen therapy (minimum O_2 9 L/min; maximum 15 L/min). Patients were excluded if they required mechanical ventilation (invasive or non-invasive) or if they had hypercapnic respiratory failure. High flow therapy was delivered using a dedicated high flow delivery system (Optiflow™, Fisher & Paykel Healthcare). In most cases settings were $FiO_2 \geq 60\%$ with an initial flow rate of 40 L/min; settings were left to the attending physician's discretion and adapted to suit individual requirements according to patient severity and tolerance to HFNC.

The capacity of HFNC to alleviate dyspnea was measured using the Borg scale and a Visual Analogue Scale (VAS). The ability of HFNC to decrease respiratory rate and to increase SpO_2 was also investigated.

Measurements were collected before HFNC initiation and at 15, 30 and 60 minutes after HFNC initiation. Arterial blood gases were sampled at the investigator's discretion. Patients were asked to rate their opinion of HFNC versus face mask therapy with regard to overall comfort and noise level. Investigators were asked to rate their opinion with regard to efficacy, preparation and setup.

RESULTS:

Of the 386 patients screened, 17 were enrolled in the study. The median age was 64 years, and 53% of patients were female. The median Simplified Acute Physiology Score II was 33 (18.5-39.5). The main causes of respiratory failure were: pneumonia (n=9); cardiogenic pulmonary edema (n=4); pneumothorax (n=1); acute asthma (n=1); pleural effusion (n=1) and septic shock (n=1). Eight patients had an initial neurological status that precluded them from evaluating HFNC efficacy via the Borg scale and VAS. Borg scale and VAS assessments were significantly improved compared with before HFNC at all time points measured ($p<0.05$), as were respiratory rate ($p<0.05$) and SpO_2 ($p<0.01$). After 60 minutes of HFNC therapy, signs of respiratory distress were significantly reduced ($p<0.05$). For those patients who had blood gas measurements taken before and during HFNC therapy, there was a significant increase in PaO_2 ($p<0.05$), but no change in PCO_2 or pH (see table).

Nine patients were admitted to the intensive care unit (ICU), and 8 remained in the hospital's short-term ED hospitalization unit. All patients admitted to the ICU continued HFNC therapy. Two of the nine patients required mechanical ventilation, and one died; the remainder recovered fully. Five patients who remained in the ED unit, all of whom had do-not-resuscitate orders, died, and the remainder were discharged.

Of the nine patients able to give an opinion on the HFNC treatment, eight rated HFNC as more comfortable than the face mask, and two said they were disturbed by the noise. All 17 caregivers involved in the study rated HFNC as more efficient than therapy via face mask. The majority (65%) of investigators found no difference between HFNC and conventional oxygen therapy with respect to setup and management; 24% rated it as less difficult, and 12% as more difficult. When asked to estimate whether their patients were more comfortable with HFNC therapy, 82% of caregivers said yes, and overall 76% of providers said they preferred HFNC over conventional therapy.

Lenglet H, Sztrymf B, Leroy C, Brun P, Dreyfuss D, Ricard J.
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VARIABLE[a]	BEFORE HFNC	HFNC + 15 MINS	HFNC + 30 MINS	HFNC + 60 MINS
Borg scale [n=9]	6 (5-7)	4 (3-4)*	4 (2-4)***	3 (2-4)***
VAS [n=9]	7 (5-8)	5 (2-6)*	4 (2-6)***	3 (1-5)**
Respiratory rate, breaths/min [n=17]	28 (25-32)	25 (23-30)*	25 (21-30)**	25 (21-28)***
SpO_2, % [n=17]	90 (89-94)	96 (90-99)**	95 (90-100)***	97 (93-100)***
Signs of respiratory distress; % [n=17]	59			18*
PaO_2, mmHg [n=6][b]	61 (56-74)			129 (96-194)*
PCO_2, mmHg [n=6][b]	40 (35-47)			40 (36-46)
pH [n=6][b]	7.4			7.4

[a] Median (inter-quartile range) unless otherwise stated.

[b] Measured before and during HFNC (at no particular time)

*p<0.05; **p<0.01; ***p<0.001

CONCLUSION:

The results of this study showed that HFNC use results in rapid and sustained improvement of dyspnea and oxygenation in patients with respiratory distress presenting to the ED. HFNC was well tolerated, and rated as more comfortable and not more difficult to use than conventional oxygen therapy delivered via face mask. In addition, acceptance by caregivers was widespread. These results show that HFNC is feasible and effective in the ED setting, and that it may be an option for first-line therapy in severe cases. Further investigation is required to determine whether HFNC could reduce the number of patients requiring admission to the ICU and mechanical ventilation.

KEY POINTS:

- Use of HFNC results in rapid and sustained improvement of dyspnea and oxygenation in patients with respiratory distress presenting to the ED.
- HFNC was well tolerated, and rated as more comfortable and not more difficult to use than conventional oxygen therapy delivered via face mask.
- HFNC is feasible and effective in the ED setting, and may be an option for first-line therapy in severe patients.
- Further investigation is required to determine whether HFNC could reduce the number of patients requiring admission to the ICU and mechanical ventilation.

inScience Communications

Lucangelo U, Vassallo F, Marras E, Ferluga M, Beziza E, Comuzzi L et al.
Crit Care Res Pract. 2012;2012:1-6.

High-flow nasal interface improves oxygenation in patients undergoing bronchoscopy.

AIM:

To compare the effects of oxygen therapy delivered via Venturi mask or high-flow nasal cannula (HFNC) on gas exchange and cardiovascular parameters in patients undergoing bronchoscopy and bronchoalveolar lavage (BAL) fluid collection for the diagnosis of pulmonary disease. In addition, the generation of continuous positive airway pressure (CPAP) during use of the different oxygen therapy systems was determined in healthy volunteers.

METHOD:

Patients aged ≥18 years with oxygen saturation (SpO_2) ≥90% and without cardiac or respiratory failure were randomized to receive oxygen during bronchoscopy by one of three different strategies: via Venturi face mask (OS/62 K; FIAB) at 40 L/min (V40), via HFNC (Fisher & Paykel Healthcare) at 40 L/min (N40) or HFNC at 60 L/min (N60). In the V40 group gas delivery was controlled using an air entrainer with Venturi effect (RT008; Fisher & Paykel Healthcare), and in the N40 and N60 groups gas delivery was controlled using a continuous high-flow generator with Venturi effect (9293/D; Harol). In all groups the inspired oxygen fraction (FiO_2) was 50%, and gases were heated and humidified using a servo-controlled heated respiratory humidifier (MR730; Fisher & Paykel Healthcare). Fibreoptic bronchoscopy (18-F; Olympus Corp.) was performed using a dedicated mouthpiece (Pentax). BAL was done using 150mL of warmed saline solution. Measurement of gas exchange and respiratory parameters was made at baseline, at the end of bronchoscopy and after a 10-minute rest period during which all patients were switched to V40. Patients rated comfort during bronchoscopy on a scale from 1 (excellent) to 4 (poor).

Volunteers underwent simulated bronchoscopy and received oxygen delivered at V40, N40 and N60. Airway pressure was measured using a catheter positioned in the pharynx.

RESULTS:

Forty-five patients (21 female & 24 male; aged 37-83 years; 15 per group) and eight volunteers (4 female & 4 male; age 25-37 years) were enrolled. Data for gas exchange and cardiovascular parameters are shown in the table. Patient comfort ratings were similar in the three treatment groups. HFNC oxygen therapy was well tolerated.

No measurable end-expiratory pressure was generated in volunteers receiving V40 or N40, but a median end-expiratory pressure of 3.6 cm H_2O was detecting with N60.

Lucangelo U, Vassallo F, Marras E, Ferluga M, Beziza E, Comuzzi L et al.
Crit Care Res Pract. 2012;2012:1-6.

MEDIAN (1ST-3RD QUARTILE)	BASELINE	END OF BRONCHOSCOPY	10 MINUTES AFTER BRONCHOSCOPY
$PaCO_2$ (mm Hg)			
V40	37.5 (35.0-42.1)	42.7 (41.0-44.4)[a]	42.2 (39.7-43.2)[a]
N40	39.1 (37.3-41.5)	43.2 (37.9-47.6)[a]	43.4 (41.0-45.7)[a]
N60	39.6 (33.4-42.5)	43.6 (42.4-48.0)[ac]	40.7 (38.0-45.5)
PaO_2/FiO_2			
V40	322.4 (295.6-374.3)	165.0 (127.4-199.2)[a]	248.6 (206.6-274.3)[ab]
N40	342.8 (295.7-371.9)	140.6 (125.6-153.6)[a]	224.3 (206.6-249.1)[ab]
N60	350.9 (304.3-363.8)	244.8 (181.6-366.8)[cd]	278.8 (222.9-304.0)[a]
a/A PO_2			
V40	0.674 (0.587-0.764)	0.265 (0.207-0.326)[a]	0.441 (0.342-0.515)[ab]
N40	0.723 (0.652-0.745)	0.224 (0.204-0.249)[a]	0.421 (0.352-0.446)[ab]
N60	0.718 (0.659-0.765)	0.401 (0.295-0.604)[acd]	0.480 (0.389-0.536)[a]
PaO_2 (mm Hg)			
V40	67.7 (62.1-78.6)	82.5 (63.7-99.6)	87.0 (72.3-101.8)
N40	72.0 (62.1-78.1)	70.3 (62.8-76.8)	78.5 (72.3-87.2)
N60	73.7 (63.9-76.4)	122.4 (90.8-183.4)[ad]	97.6 (78.0-106.4)[ab]
SpO_2 (%)			
V40	94 (93-96)	94 (92-96)	95 (92-98)
N40	95 (91-96)	92 (90-95)	93 (91-95)
N60	95 (93-97)	98 (97-99)[acd]	95 (95-98)[bc]
HR (beats/min)			
V40	75.0 (62.0-97.0)	90 (76-110)[a]	82.0 (75.0-90.0)[b]
N40	78.0 (72.0-85.0)	84 (80-101)	80.0 (79.0-91.0)[a]
N60	74.0 (68.0-84.0)	84 (70-100)[a]	76.0 (64.0-89.0)[b]
MAP (mm Hg)			
V40	94.0 (90.0-107.0)	108.0 (92.0-126.0)	91.0 (83.0-103.0)
N40	102.0 (92.0-112.0)	99.0 (94.0-105.0)	94.0 (85.0-98.0)[b]
N60	109.0 (100.0-117.0)	103.0 (93.0-117.0)	96.0 (87.0-108.0)

[a] $p<0.05$ vs baseline; [b] $p<0.05$ vs during bronchoscopy; [c] $p<0.05$ vs V40; [d] $p<0.05$ vs N40.

a/A PO_2, ratio between arterial and alveolar oxygen pressure; HR, heart rate; MAP, mean arterial pressure; $PaCO_2$, arterial pressure of carbon dioxide; PaO_2/FiO_2, ratio between arterial oxygen pressure and inspiratory fraction of oxygen; SpO_2, peripheral oxygen saturation.

DISCUSSION:

This appears to be the first study investigating the effect of HFNC oxygen therapy on gas exchange and cardiovascular parameters in patients undergoing bronchoscopy and BAL. Gas exchange is usually impaired during bronchoscopy as a result of sedation and ventilation-perfusion mismatch. The significant improvements observed in gas exchange during HFNC oxygen therapy at a rate of 60 L/min may be due to the low level of CPAP generated during therapy.

CONCLUSION:

HFNC oxygen therapy at a flow rate of 60 L/min significantly improved oxygenation during bronchoscopy and recovery compared with oxygen therapy delivered via a face mask at 40 L/min.

KEY POINTS:

- HFNC oxygen therapy at 60 L/min improves oxygenation during bronchoscopy and recovery.
- HFNC oxygen therapy at 60 L/min generates a low level of CPAP.
- CPAP generation during HFNC oxygen therapy at 60 L/min may contribute to improved oxygenation.

inScience Communications

STUDY 4 | **Parke R, McGuinness S, Eccleston M.**
Respir Care. 2011;56(3):265-270.

A preliminary randomized controlled trial to assess effectiveness of nasal high-flow oxygen in intensive care patients.

AIM:

To compare the effectiveness and tolerability of nasal high flow (NHF) oxygen therapy and standard high-flow face mask (HFFM) oxygen therapy in patients with mild-to-moderate hypoxaemic respiratory failure in the intensive care unit (ICU).

METHOD:

In this prospective, single-centre study, 60 ICU patients with mild-to – moderate hypoxaemic respiratory failure were randomized to receive humidified high-flow oxygen via either a NHF system (Optiflow, with MR880 humidifier, RT241 heated delivery tube, RT033 or RT034 nasal cannula; Fisher & Paykel Healthcare) or a HFFM system (standard face mask, MR850 humidifier, RT308 heated delivery tube and air entrainer; Fisher & Paykel Healthcare) and an aerosol mask (Hudson RCI; TFX Medical). NHF was initiated at a flow rate of 35 L/min, and then flow and the inspired oxygen fraction (FiO_2) were titrated to achieve an oxygen saturation by pulse oximetry (SpO_2) or arterial blood gas (SaO_2) of ≥95%. Patients in the HFFM group received oxygen at 31°C and 32 mg H_2O/L also titrated to achieve SpO_2 or SaO_2 of ≥95%. Variables assessed were rate of transfer to noninvasive ventilation (NIV), the partial pressure of arterial oxygen (PaO_2)/FiO_2 ratio, SpO_2 and length of hospital stay.

Patients who failed on their randomized therapy (defined as worsening respiratory failure that required a change in the respiratory support device within 24 hours after enrollment) were treated at the physician's discretion.

RESULTS:

Data from 56 patients were available for analysis; there were no significant differences between the two treatment groups in baseline demographics. Therapy success and desaturation data are reported in the table below. There was no significant difference between the two groups in PaO_2/FiO_2, time to ICU discharge or hospital stay.

DISCUSSION:

NHF has been shown to have good patient acceptability and to provide effective oxygenation. Potential explanations for the clinical benefit observed in this study include generation of positive airway pressure and washout of anatomical deadspace. Furthermore, humidification of inspired gases during long-term respiratory therapy has been shown to improve lung function and decrease exacerbations, as well as contributing to patient comfort. Limitations of this study include availability of desaturation data in only a subset of patients, and desaturation data were not detailed enough to perform a comprehensive analysis.

	NHF	HFFM	P VALUE
Success on allocated therapy (patients)	26/29	15/27	0.006
NIV required (patients)	3/29	8/27	0.10
≥1 desaturation (patients)	8/19	10/14	0.16
Mean number of desaturation episodes	15	26	0.009
Mean desaturations per patient	0.79	1.86	
Mean desaturations per hour	0.21	0.47	

HFFM = high-flow face mask; NHF = nasal high flow therapy; NIV = noninvasive ventilation.

CONCLUSION:

NHF was more successful than HFFM for the treatment of ICU patients with mild-to-moderate respiratory failure.

KEY POINTS:

- NHF oxygen therapy is more successful than HFFM oxygen therapy in ICU patients with mild-to-moderate respiratory failure.
- NHF oxygen therapy has an increasing role as an option for respiratory therapy in the ICU.

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STUDY 5 | **Peters S, Holets S, Gay P.**
Respir Care. 2013 ; 58(4): 597-600.

Nasal high flow oxygen therapy in do-not-intubate patients with hypoxemic respiratory distress.

AIM:

To assess the effectiveness of high-flow nasal cannula (HFNC) oxygen therapy in Do-Not-Intubate (DNI) patients with hypoxaemia and mild hypercapnia.

METHOD:

The medical records of patients receiving HFNC oxygen therapy in the medical or medical-surgical intensive care unit (ICU) between May 2009 and May 2011 were retrospectively analyzed. Patients had clinical evidence of respiratory distress, hypoxaemia and mild or compensated hypercapnia (arterial carbon dioxide pressure [$PaCO_2$] ≤65 mm Hg, pH >7.28) and a Do-Not-Resuscitate or DNI status. HFNC oxygen therapy was delivered using the Optiflow™ system (Fisher & Paykel Healthcare), which included the MR850 respiratory humidifier plus a chamber, heated delivery tubing, and a small or large bore nasal cannula. Therapy was initiated at a flow rate of 35 L/min and titrated up to 45-60 L/min if tolerated. The fraction of inspired oxygen (FiO_2) was titrated to maintain arterial oxygen saturation (SaO_2) at >90% or as determined by the clinician. The primary endpoint was need for escalation to noninvasive ventilation (NIV). Ventilation and gas exchange parameters (secondary endpoints) were extracted using the closest values prior to initiation of HFNC oxygen therapy and approximately 1 hour later.

Patient tolerance of HFNC oxygen therapy was also assessed.

RESULTS:

Fifty patients (25 male & 25 female; age 27-96 [mean 73] years) were included. Flow rate during therapy was 30-60 (mean 42.6) L/min. Arterial blood gas data were only available in 23 patients after initiation of HFNC oxygen therapy. Duration of NFNC oxygen therapy was 2-144 hours (mean 41.9 hours, median 30 hours).
Data on primary and secondary endpoints are shown in the table. No patient reported nasal bleeding or facial skin breakdown during HFNC oxygen therapy.

	BEFORE HFNC	HFNC
PaO_2 (mm Hg)	66.5 (39-121)	95.4
$PaCO_2$ (mm Hg)	42.3 (26-65)	40.2
pH	7.42 (7.30-7.51)	7.43
Respiratory rate (breaths/min)	30.6	24.7[a]
Oxygen saturation (%)	89.1	94.7[a]
Escalation to NIV [patients(%)]		9/50 (18%)

Values are means unless otherwise stated, followed by range where data available.

[a] p<0.001 vs before HFNC oxygen therapy.

HFNC, high-flow nasal cannula oxygen therapy; NIV, noninvasive ventilation; $PaCO_2$, arterial pressure of carbon dioxide; PaO_2, arterial pressure of oxygen.

DISCUSSION:

Patients with a DNI order are often transferred to the ICU specifically for initiation of NIV. Although this study was conducted in ICU patients, it is possible that the use of HFNC oxygen therapy might allow delivery of adequate oxygenation without the requirement for admission to the ICU. The rate of progression to NIV in this series of relatively ill patients was quite low at 18%.

CONCLUSION:

Use of HFNC oxygen therapy improved oxygenation and respiratory rate in patients with hypoxaemic respiratory distress, with a low rate of progression to NIV.

KEY POINTS:

- HFNC oxygen therapy improves oxygenation and the respiratory rate in DNI patients with respiratory distress.
- HFNC oxygen therapy is well tolerated in DNI patients with respiratory distress.
- Use of HFNC oxygen therapy in DNI patients with respiratory distress has a low rate of progression to NIV.

inScience Communications

STUDY 6 | **Rea H, McAuley S, Jayaram L, Garrett J, Hockey H, Storey L et al.**
Respir Med. 2010;104(4):525-533.

The clinical utility of long-term humidification therapy in chronic airway disease.

AIM:

To compare long-term humidification therapy (LTHT) with usual care on the frequency of exacerbations, lung function, quality of life and exercise capacity in adults with chronic airway disease.

METHOD:

Patients with chronic obstructive pulmonary disease (COPD) or bronchiectasis entered this prospective, randomised, single centre, open-label 12-month study. Those in the LTHT group (n = 60) were to use the LTHT device for ≥2 hours every day at home; concomitant usual therapy (e.g. corticosteroids, oral antibiotics) was allowed. The other group continued to receive their usual treatment (n = 48).

The Optiflow™ [Fisher & Paykel Healthcare] device, consisting of Optiflow™ nasal cannulae connected to an MR880 humidifier and HC210 flow source system, was used to deliver humidified air, fully saturated at 37 °C. Patients selected a flow rate of either 20 or 25 L/min.

Patients recorded exacerbations in their diaries; an exacerbation was defined as worsening of two or more respiratory symptoms for two or more days requiring treatment. Three blinded investigators adjudicated exacerbation data. Dyspnoea and quality of life were self-reported, using the Medical Research Council (MRC) Scale, and the St George's Respiratory Questionnaire (SGRQ), respectively. Lung function (using spirometry) and exercise capacity (using the 6 minute walk distance test [6MWD]) were also assessed.

RESULTS:

There was no significant difference between groups in exacerbation frequency, with 3.63 exacerbations/patient/year in the usual care group and 2.97 in the LTHT group (primary endpoint; p=0.067). However, the number of exacerbation days was significantly lower, and the median time to first exacerbation significantly longer, in the LTHT group (table).

Differences in the following lung function parameters were significant (all p<0.05) and favoured the LTHT group at 3 and 12 months: forced expiratory volume in 1 second (FEV1), percentage of predicted FEV1, forced vital capacity (FVC) and percentage of predicted FVC. The FEV1/FVC ratio did not change significantly from baseline in either group at 3 months or 12 months.

The SGRQ total score was significantly (p<0.05) lower (indicating improvement vs baseline) in the LTHT group than the usual care group at 3 and 12 months, with differences in score of at least 5.9 points at 12 months (4 points is considered to be clinically meaningful).

No significant difference was seen in exercise capacity.

Except for antibiotic use, which was significantly (p=0.008) lower in the LTHT group, overall medication use was similar between the groups.

Most LTHT patients used the device for ≥1 hour/day (80% [48/60]) and 32% [19/60] used it for ≥2 hours/day). Mean (standard deviation [SD]) use per day per patient was 1.6 (0.67) hours.

There were no serious adverse events related to study therapy.

Rea H, McAuley S, Jayaram L, Garrett J, Hockey H, Storey L et al.
Respir Med. 2010;104(4):525-533.

VARIABLES	LTHT	USUAL CARE	RATIO	VARIABLES
SELECTED SECONDARY ENDPOINTS				
No. of days of exacerbation over 12 months (geometric mean)	18.2	33.5	0.544 (0.300, 0.985)	0.045
No. of days to first exacerbation (predicted median)	52	27	0.650* (0.423, 0.999)	0.050
Pts with no exacerbations, n (%)	12/60 (20.0%)	4/48 (8.3%)	NA	0.043
MRC dyspnoea scores at 12 months (mean)	2.49	2.54	NA	0.518
% change from baseline in 6MWD at 12 months	−4.0	−8.6	NA	0.485

% = percentage; 6MWD = 6 minute walking distance test; CI = confidence interval; LTHT = long-term humidification therapy; mo = month; MRC = Medical Research Council; NA = not applicable; no. = number; pts = patients.

* = Hazard ratio

DISCUSSION:

COPD and bronchiectasis are chronic airway disorders characterised by excess mucous production and recurrent infective exacerbations. COPD and bronchiectasis are associated with with concomitant decline in lung function and quality of life. This is the first long-term study of LTHT in patients with COPD or bronchiectasis. The primary endpoint was not met, possibly because the study was under-powered or that patients with both COPD and bronchiectasis were included. However, the 18.2% reduction in exacerbation rate with LTHT is within the range (15-25%) observed with best medical therapy (e.g. with inhaled corticosteroids, long-acting β agonists and tiotropium).

This study did demonstrate that 1-2 hours/day of LTHT significantly reduced the number of exacerbation days and increased the time to first exacerbation compared with usual care. It is postulated that LTHT enhances lung mucociliary clearance, which is also suggested indirectly by the improvement in FEV1 and FVC without any change in the FEV1/FVC ratio. Further investigation of the mechanism of improvement is required.

Study results are to be interpreted with some caution since a placebo control was not feasible because none could be designed that would be undetectable by the patient. Compliance with LTHT was poorer than expected, with a mean of 1.6 hours/day versus 2 hours/day. Finally, differences in outcomes between patient subpopulations were not determined, and this remains an area for further research.

CONCLUSION:

Daily LTHT for between 1 and 2 hours in patients with COPD or bronchiectasis led to significant improvement in the number of days with exacerbations, the time to first exacerbation, lung function and quality of life. This therapy was well tolerated.

KEY POINTS:

Patients with COPD or bronchiectasis experienced significant improvements with LTHT in the number of days with exacerbations over a 12-month period, and a longer time to the first exacerbation, as compared with usual medical care.

Daily LTHT of between 1 and 2 hours with Optiflow™ may improve lung function and quality of life.

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STUDY 7 | **Roca O, Riera J, Torres F.**
Respir Care. 2010;55(4):408-413.

High-flow oxygen therapy in acute respiratory failure.

AIM:

To compare the subjective comfort of oxygen therapy given via conventional face mask (FM) versus nasal high flow (NHF) cannula (Optiflow™; Fisher & Paykel Healthcare) in patients with acute respiratory failure (ARF).

METHOD:

In this prospective, comparative study of sequential interventions, adult patients with ARF (defined as a blood oxygen saturation [SpO_2] <96% while receiving humidified oxygen via FM with a fraction of inspired oxygen [FiO_2] of ≥0.5) were given FM oxygen therapy humidified with a bubble humidifier (Respiflo Water and MN Adapter; Tyco Healthcare) for 30 minutes. Patients were then switched to NHF oxygen therapy for 30 minutes at an initial flow rate of 20–30 L/min, with a FiO_2 identical to that with the FM.

Perceived comfort (dyspnoea, mouth dryness and overall comfort) was assessed by the patients at the end of each 30-minute treatment period using a visual analogue scale (VAS) ranging from 0 (lowest) to 10 (highest). Arterial blood gas values, acid-base balance, respiratory rate and SpO_2 were also measured at this time. At the end of both 30-minute periods, patients were asked which oxygen delivery system they wanted to keep using.

RESULTS:

Twenty patients (median age 57 years; 14 males) were included in this study. The median duration of ARF was 4 (interquartile range 3–8) days prior to inclusion in the study, and 95% of patients were admitted to the intensive care unit due to hypoxaemic ARF. Data for the primary and secondary endpoints are reported in the table. After 30 minutes of FM oxygen therapy there were no significant differences in respiratory values from baseline. In contrast, a significant increase in the partial pressure of oxygen (PaO_2) and a reduction in respiratory rate without hypercapnia or acidosis was observed after 30 minutes of NHF oxygen therapy. NHF oxygen therapy was generally well tolerated. Five patients (25%) reported some mild adverse effects possibly related to NHF oxygen therapy. The most common effect, reported by three patients, was cervical-thoracic discomfort which occurred during the initial period of increasing flow that disappeared when flow was decreased, and one patient reported that the gas temperature was too high. All of these adverse effects were reported early in the testing period and disappeared before the end of the 30-minute testing period. Other mild adverse events were nonspecific nasal discomfort and nasal mucosal lesions in one patient. Nasal mucosal lesions were observed before the initiation of NHF oxygen therapy in another patient and were considered probably related to prior use of a conventional nasal cannula.

DISCUSSION:

This is the first study investigating the delivery of humidified NHF oxygen therapy in patients with ARF. NHF oxygen therapy was associated with significantly less dyspnoea and mouth dryness, and greater overall comfort compared with FM oxygen therapy. Patients found NHF oxygen therapy significantly more comfortable, and there may be several reasons for this. The improvements in dyspnoea and mouth dryness played a part in improving patient-reported comfort. In addition, unlike FM oxygen therapy, NHF oxygen therapy does not affect speaking and allows food ingestion, and this could also contribute to improved patient comfort. After the testing period, all patients chose to continue with the NHF system.

NHF oxygen therapy was also associated with greater oxygenation and a lower respiratory rate than FM oxygen therapy. The improvements in oxygenation are an important effect of NHF oxygen therapy. Although FiO_2 was not measured in this study, greater oxygenation during NHF oxygen therapy may be a result of higher FiO_2 secondary to the higher flow rate. Furthermore, the NHF oxygen therapy heated humidifier system may have indirectly affected oxygenation and also might attenuate the development of bronchial hyper-response symptoms. The adverse effects observed with NHF oxygen therapy were mild and the system can be considered comfortable as was apparent from all patients choosing to continue with NHF oxygen therapy after the testing period.

Roca O, Riera J, Torres F.
Respir Care. 2010;55(4):408-413.

	OXYGEN THERAPY		P VALUE
	NHF	FM	
SUBJECTIVE EVALUATION (VAS SCORE)			
Dyspnoea	3.8 (1.3–5.8)	6.8 (4.1–7.9)	0.001
Mouth dryness	5 (2.3–7.0)	9.5 (8.0–10.0)	<0.001
Overall comfort	9.0 (8.0–10.0)	5.0 (2.3–6.8)	<0.001
RESPIRATORY AND GAS EXCHANGE VARIABLES			
Total oxygen flow (L/min)	30.0 (21.3–38.7)	15.0 (12.0–20.0)	<0.001
Fraction of delivered oxygen	1.0 (0.8–1.0)	1.0 (0.8–1.0)	0.32
Respiratory rate (breaths/min)	21 (18–27)	28 (25–32)	<0.001
pH	7.44 (7.38–7.50)	7.42 (7.38–7.47)	0.06
PaO_2 (mm Hg)	127 (83–191)	77 (64–88)	0.002
$PaCO_2$ (mm Hg)	37 (32–43)	37 (33–45)	0.51
HCO_3 (mmol/L)	24.5 (22.2–29.1)	25.0 (22.1–28.5)	0.09
Base excess (mmol/L)	-1.0 (-2.3–5.3)	1.0 (-2.3–4.8)	0.055
SpO_2 (%)	98 (96–99)	95 (91–97)	0.002
HAEMODYNAMIC VARIABLES			
Mean arterial pressure (mm Hg)	86 (71–93)	87 (76–94)	0.36
Heart rate (beats/min)	85 (73–108)	94 (77–112)	>0.99

All values are median and interquartile range; FiO_2 = fraction of inspired oxygen; HCO3– = blood bicarbonate; IQR = interquartile range; PaO_2 = partial pressure of oxygen; $PaCO_2$ = partial pressure of carbon dioxide; SpO_2 = blood oxygen saturation as measured via pulse oximetry.

CONCLUSION:

NHF oxygen therapy is considered by patients to be more comfortable than FM oxygen therapy, and is better tolerated and more effective in the management of ARF. Further investigation is needed to determine the clinical scenarios in which its benefits will have the greatest impact.

KEY POINTS:

- NHF oxygen therapy is associated with significantly less dyspnoea and mouth dryness, and greater overall comfort compared with FM oxygen therapy in patients with ARF.
- NHF oxygen therapy improves oxygenation and respiratory rates compared with FM oxygen therapy in patients with ARF.
- NHF oxygen therapy could play an important role in the integrated treatment of patients with ARF.

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STUDY 8

Roca O, Pérez-Terán P, Masclans J, Pérez L, Galve E, Evangelista A et al.
J Crit Care. 2013;28(5):741-746.

Patients with New York Heart Association class III heart failure may benefit with high flow nasal cannula supportive therapy.

High flow nasal cannula in heart failure.

AIM:

To investigate whether the use of high flow nasal cannula (HFNC) in patients with heart failure (HF) is associated with a decrease in preload with no change in cardiac output (i.e., hemodynamic improvement).

METHOD:

This was a sequential interventional study conducted at Vall d'Hebron University Hospital in Spain. Inclusion criteria were: stable heart failure (HF) with New York Heart Association (NYHA) functional class III, at least one hospital admission in the 12 months prior to enrollment, and a left ventricular ejection fraction ≤45%. Stable HF was defined as the absence of decompensation (a change in HF symptoms requiring urgent therapy). Patients received humidified HFNC (Optiflow™, Fisher & Paykel Healthcare) in two consecutive 30 minute periods, at flow rates of 20 and 40 L/min in the first and second periods, respectively. The fraction of inspired oxygen (FiO_2) was set at 0.21, and medium cannulae were used in all patients. Patients underwent transthoracic echocardiography at baseline, at the end of each 30 minute period, and 30 minutes after HFNC was stopped. Other variables recorded included: heart rate, blood pressure, respiratory rate and pulse oximetry.

RESULTS:

Ten patients were enrolled in the study. The median age was 57 years, 60% were female and the most frequent reason for HF was dilated cardiomyopathy (8 of 10 patients). Median inferior vena cava (IVC) inspiratory collapse decreased from 37% at baseline to 28% and 21% after HFNC therapy at flow rates of 20 and 40 L/min, respectively ($p<0.05$), a mean reduction of 20% (95% confidence interval [CI] 6-55) and 53% (95% CI 36-67); changes were significantly greater with a flow rate of 40 L/min versus 20 L/min ($p=0.03$). IVC inspiratory collapse changes reversed once HFNC was withdrawn. Respiratory changes are summarized in the table. Respiratory rate also returned to baseline levels upon withdrawal of HFNC, and a significant inverse correlation between HFNC flow and respiratory rate was found ($r= -0.57$; $p<0.001$). There were no significant changes in the other parameters measured.

VARIABLE	BASELINE	HFNC 20 L/MIN	HFNC 40 L/MIN
Median respiratory rate, breaths/min	23	17	13*

*p=0.02

Roca O, Pérez-Terán P, Masclans J, Pérez L, Galve E, Evangelista A et al.
J Crit Care. 2013;28(5):741-746.

CONCLUSION:

This study is the first to describe the hemodynamic changes that occur when patients with HF are treated with HFNC. The results suggest that treatment with HFNC may be associated with a decrease in preload (as measured by IVC inspiratory collapse), with no change in ventricular function in patients with NYHA functional class III HF. HFNC treatment also significantly decreased respiratory rate in these patients.
The authors hypothesized that the IVC-related changes during HFNC therapy could be related to an increase in lung volume and/or an increase in intrathoracic pressure. The decrease in respiratory rate seen may be related to a wash-out effect of the upper respiratory airway leading to a reduction in anatomical dead space, or to an increase in tidal volume.

KEY POINTS

- The results of this study show that patients with NYHA III HF may gain hemodynamic benefits from treatment with HFNC.
- Respiratory rate decreased from baseline during HFNC treatment.
- Respiratory rate returned to baseline upon withdrawal of HFNC, and a significant inverse correlation between HFNC flow and respiratory rate was found.

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STUDY 9

Sztrymf B, Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D et al.
Intensive Care Med. 2011;37(11):1780-1786

Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study.

AIM:

To investigate the effects of high-flow nasal cannula (HFNC) oxygen therapy on respiratory parameters and outcomes in intensive care unit (ICU) patients with acute respiratory failure (ARF).

METHOD:

This prospective, observational study included patients admitted to the ICU for ARF or persistent signs of respiratory distress. All patients were switched from conventional oxygen therapy given via a high fraction of inspired oxygen (FiO_2) nonrebreathing facemask (Hudson RCI; Teleflex Medical) to HFNC oxygen therapy given using the Optiflow™ system (Fisher & Paykel Healthcare). All procedures were part of routine clinical care.

Respiratory, haemodynamic and clinical variables were assessed at baseline and at specific times over the first 48 hours after switching to HFNC. Arterial blood gases were measured at baseline and after 1 and 24 hours.

Device noise and patient discomfort were measured throughout HFNC oxygen therapy using a visual numeric scale ranging from 0-10.

RESULTS:

Thirty-eight patients (mean age 54.2 years) were included. The mean Simplified Acute Physiology Score (SAPS II) was 39 ± 10. The three most common causes of ARF were community-acquired pneumonia (n = 15), H1N1 influenza infection (n = 5) and cardiogenic pulmonary oedema (n=5). Mean duration of HFNC therapy was 2.8 ± 1.8 days.

Compared to baseline, switching to HFNC oxygen therapy was associated with statistically significant reductions in respiratory rate (p = 0.009) and pulse oximetry (p <0.005) after 15 min, and in dyspnoea score, supraclavicular retraction and thoracoabdominal asynchrony after 30 min (all p < 0.05). Statistically significant reductions in heart rate were seen 6 hours after switching to HFNC.

Changes in arterial blood gases are reported in the following table.

MEAN ± SD	BASELINE	HFNC OXYGEN THERAPY		P VALUE
		1h	24h	
PaO_2 (mm Hg)	141 ± 106	95 ± 40		0.009
PaO_2/FiO_2 ratio	169 ± 108	187 ± 86	102 ± 23	0.036
$PaCO_2$ (mm Hg)	38 ± 11	37 ± 11	38 ± 10	0.77
pH	7.43 ± 0.09	7.44 ± 0.07	7.41 ± 0.07	0.87

FiO_2 = fraction of inspired oxygen; PaO_2 = partial pressure of oxygen; $PaCO_2$ = partial pressure of carbon dioxide; SD = standard deviation.

Sztrymf B, Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D et al.
Intensive Care Med. 2011;37(11):1780-1786

There was no change in noise or nasal discomfort scores from the beginning to the end of the study. No patient discontinued NFHC oxygen therapy because of intolerance. Secondary intubation and mechanical ventilation was required in 9 patients. Significant predictors of intubation were no decrease in respiratory rate, a high level of thoracoabdominal asynchrony, and lower SpO_2, PaO_2 and PaO_2/FiO_2 ratio after initiation of HFNC oxygen therapy.

DISCUSSION:

HFNC oxygen therapy is widely used in neonates, but fewer data are available on its usefulness in adults. Data from this prospective trial confirm that HFNC is well tolerated in adults, and is associated with early, sustained and beneficial effects on oxygenation and clinical parameters. In addition, predictors that may assist in identifying patients who are most likely to require intubation were identified. The results indicated that non-invasive ventilation, or intubation and mechanical ventilation, might be avoided in more than 75% of patients receiving HFNC. This pilot study provides sufficient rationale to justify conducting a randomized controlled clinical trial to investigate the potential of HFNC oxygen therapy to reduce the intubation rate in patients with hypoxaemic ARF.

CONCLUSION:

HFNC oxygen therapy had a beneficial effect on oxygenation and clinical outcomes in patients with ARF in the ICU.

KEY POINTS:

- HFNC oxygen therapy is associated with early and sustained beneficial effects on clinical respiratory parameters in patients with acute respiratory failure.
- HFNC oxygen therapy improves oxygenation in adult ICU patients with acute respiratory failure.
- HFNC oxygen therapy is well tolerated in adult ICU patients with acute respiratory failure.
- HFNC oxygen therapy may be associated with a reduction in the requirement for mechanical ventilation.
- Respiratory rate may be a useful early predictor of HFNC oxygen therapy failure.

inScience Communications

Maggiore S, Idone F, Vaschetto R, Festa R, Cataldo A, Antonicelli F et al.
Am J Respir Crit Care Med. 2014;190(3):282-288.

Nasal high-flow vs Venturi mask oxygen therapy after extubation: effects on oxygenation, comfort and clinical outcome.

AIM:

To compare the effect of nasal high flow (NHF) to the Venturi mask upon PaO_2/FiO_2SET ratios in post extubation patients. Comfort, adverse events and clinical outcomes were secondary study endpoints.

METHOD:

Patients (n=105) from two Italian intensive care units (ICUs) that had been mechanically ventilated for >24 hours were eligible for enrolment if they passed a spontaneous breathing trial, and had a PaO_2 to fraction of inspired oxygen (FiO_2) ratio of ≤300 at the end of the trial. Immediately after extubation, patients were randomised to receive oxygen therapy via Venturi mask (n = 52) or NHF system (n = 53) (Optiflow™; Fisher & Paykel Healthcare) for 48 hours or until ICU discharge. In both groups, the set FiO_2 (FiO_2SET) was adjusted to maintain arterial oxygen saturation (SaO_2) between 92–98% (or 88–95% in patients with compensated hypercapnia). The gas flow rate was set at 50 L/min for NHF. Arterial blood gases, SaO_2, FiO_2SET, respiratory rate, mean arterial pressure, heart rate and patient discomfort were recorded at 1, 3, 6, 12, 24 and 48 hours. The levels of discomfort for both interface and symptoms of airway dryness were rated on a scale from 0 (no discomfort) to 10 (maximum discomfort).

RESULTS:

Key treatment group data (NHF compared to Venturi mask) are shown in the table. After 24 hours, PaO_2/FiO_2SET ratio was significantly improved with NHF. In addition, both respiratory rate and arterial carbon dioxide tension ($PaCO_2$) were lower in the NHF group at all timepoints. The mean between-group difference in respiratory rate was 4±1 breaths/min (p≤0.01); however, the only statistically significant difference in $PaCO_2$ was seen at 3 hours (p=0.04). Heart rate and mean arterial pressure were similar between groups at all times. Interface-related and dryness-related discomfort was significantly lower on NHF (from 12 hours and 24 hours onwards, respectively (see table). Adverse events and clinical outcomes data favoured NHF over Venturi mask (see table).

CONCLUSION:

The results of this study show that use of NHF after extubation results in an improved PaO_2/FiO_2SET ratio for the same set FiO_2 compared to Venturi mask. In addition, NHF has shown to decrease respiratory rate and the number of oxygen desaturation episodes, improve patient comfort, and reduce the need for noninvasive ventilation or reintubation compared to oxygen therapy via Venturi mask.

There are a number of proposed NHF mechanisms for these outcomes: provision of consistent % FiO_2 by delivering gas at flow rates exceeding the patient's peak inspiratory demand; creation of an oxygen reservoir within the upper airway as a result of upper airway dead space washout by high gas flow; and the ability to generate low levels of positive airway pressure. Inclusion of heated humidification provided by the NHF system is believed to make an important contribution to improving patient comfort, particularly with respect to symptoms of airway dryness. This improved comfort is conceivably associated with less interface displacement and may contribute to the reduction in oxygen desaturation episodes seen in the NHF group.

Given the suggested improvement in preventing reintubation in this study, further investigation is warranted.

Maggiore S, Idone F, Vaschetto R, Festa R, Cataldo A, Antonicelli F et al.
Am J Respir Crit Care Med. 2014;190(3):282-288.

VARIABLE	OXYGEN THERAPY		P-VALUE
	Venturi mask (n=52)	NHF (n=53)	
OXYGENATION			
PaO_2/FiO_2SET, mmHg			
24 hours	247.4 ± 80.6	287.2 ± 74.3	0.03
36 hours	233.2 ± 75.8	310.8 ± 87.7	0.0003
48 hours	250.2 ± 110.1	313.3 ± 83.8	0.01
PaO_2, mmHg[a]	85.4 ± 16.3	97.5 ± 29.2	0.04
FiO_2SET, %[b]	39.3 ± 9.1	35.1 ± 8	0.014
DRYNESS-RELATED COMFORT SCORE[bc]			
Mouth dryness	5.0 ± 3.1	3.6 ± 2.5	0.016
Throat dryness	4.5 ± 3.3	2.7 ± 2.4	0.002
Difficulty swallowing	4.1 ± 3.4	2.5 ± 2.6	0.007
Throat pain	3.1 ± 3.4	1.7 ± 2.1	0.008
ADVERSE EVENTS & CLINICAL OUTCOMES			
Interface displacement, episodes/pt	1.7	0.4	<0.001
Pts with interface displacement, n (%)	29 (55.8)	17 (32.1)	0.01
Oxygen desaturation, episodes/pt	3.4	0.8	<0.001
Pts with oxygen desaturation[d]**, n (%)**	39 (75)	21 (39.6)	<0.001
POST-EXTUBATION ARF REQUIRING VENTILATOR SUPPORT, N (%)			
Noninvasive ventilation	8 (15.4)	2 (3.8)	0.042
Endotracheal intubation	11 (21.2)	2 (3.8)	0.005
Length of stay in the ICU, days	10.4 ± 8.5	11.7 ± 10.2	0.44
Mortality at ICU discharge, %	9.6	11.3	0.77

Values are mean ± standard deviation, unless otherwise stated.

[a] Value at 36 hours; [b] Average value over the 48-hour study period; [c] on a scale from 0 (no discomfort) to 10 (maximum discomfort); [d] Oxygen desaturation detected electronically.

ARF, acute respiratory failure; FiO_2SET, set inspired oxygen fraction; ICU, intensive care unit; PaO_2, arterial oxygen tension; patient.

KEY POINTS

- Use of NHF post extubation results in better oxygenation for the same set FiO_2 compared to oxygen therapy via Venturi mask.
- Use of NHF post extubation may decrease the respiratory rate and the number of oxygen desaturation episodes compared to oxygen therapy via Venturi mask.
- Post extubation, NHF may be associated with improved patient comfort compared with oxygen therapy via Venturi mask, particularly regarding symptoms of airway dryness.
- In recently extubated patients, NHF may reduce the need for noninvasive ventilation or reintubation compared to oxygen therapy via Venturi mask.

inScience Communications

Frat J, Thille A, Mercat A, Girault C, Ragot S, Perbet S et al.
N Engl J Med. 2015;372(23):2185-2196.

High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure.

AIM:

To compare the use of standard oxygen therapy, nasal high-flow (NHF) oxygen therapy and noninvasive ventilation (NIV) in patients admitted to the intensive care unit (ICU) with acute hypoxemic respiratory failure with respect to intubation rate, mortality and other clinical outcomes.

METHOD:

This 23-center, prospective, randomized trial included patients who had acute hypoxemic respiratory failure without hypercapnia, a ratio of partial pressure of arterial oxygen (PaO_2) to fraction of inspired oxygen (FiO_2) of ≤300 mmHg, a partial pressure of carbon dioxide ($PaCO_2$) ≤45 mmHg and a respiratory rate >25 breaths/minute. All patients were randomized in a 1:1:1 ratio, and oxygen was adjusted to achieve oxygen saturation (SaO_2) of ≥92%. Patients received either standard oxygen therapy via a nonrebreather face mask at ≥10 L/min, NHF oxygen therapy via large-bore nasal prongs (Optiflow™, Fisher & Paykel Healthcare) with heated humidification (MR850™, Fisher & Paykel Healthcare) at a rate of 50 L/min and an initial FiO_2 of 1.0, or NIV via a face mask (Fisher & Paykel Healthcare) connected to an ICU ventilator with pressure support applied in NIV mode. The pressure support level was adjusted with the aim of obtaining an expired tidal volume of 7–10 mL/kg of predicted body weight, with an initial positive end-expiratory pressure (PEEP) of 2–10 cmH_2O; FiO_2 and/or PEEP were adjusted as above. NHF oxygen therapy was applied for at least 2 days and the minimum required duration of NIV was 8 hours/day for 2 days. The primary endpoint was the proportion of patients requiring endotracheal intubation within 28 days after randomization. Secondary outcomes were mortality in the ICU and at 90 days, the number of ventilator-free days from day 1 to day 28, and duration of ICU stay.

RESULTS:

A total of 313 patients were randomized between February 2011 and April 2013; 310 patients were included in the analysis after three patients withdrew consent (94 received standard oxygen therapy, 106 received NHF oxygen therapy and 110 received NIV). For the majority of patients (64%), the cause of acute respiratory failure was community-acquired pneumonia.

Key primary and secondary endpoint data are summarized in the table. Compared with the NHF oxygen therapy group, the hazard ratio (HR) for intubation at day 28 overall was 1.45 (95% confidence interval [CI] 0.83 - 2.55) in the standard oxygen therapy group and 1.65 (95% CI 0.96 - 2.84) in the NIV group. In a subgroup analysis of patients with PaO_2:FiO_2 ≤200 mmHg corresponding values were 2.07 (95% CI 1.09 - 3.94) and 2.57 (1.37- 4.84) in the unadjusted analysis, and 2.14 (95% CI 1.08 - 4.22) and 2.60 (95% CI 1.36 - 4.96) after adjustment for bilateral pulmonary infiltrates, respiratory rate and history of cardiac insufficiency. The unadjusted HR for death at 90 days in the standard versus NHF oxygen therapy group was 2.01 (95% CI 1.01- 3.99; p=0.046) and in the NIV versus NHF group was 2.50 (95% CI 1.31- 4.78; p=0.006). In the adjusted analysis, corresponding values were 2.36 (95% CI 1.18 - 4.70) and 2.33 (1.22 - 4.47).

There was no statistically significant difference between treatment groups in the rate of serious adverse events. At 1 hour after initiation of treatment, patients in the NHF oxygen therapy group had less respiratory discomfort and lower dyspnea scores compared with the other two groups.

Frat J, Thille A, Mercat A, Girault C, Ragot S, Perbet S et al.
N Engl J Med. 2015;372(23):2185-2196.

VARIABLE	STANDARD OXYGEN THERAPY (N=94)	NHF OXYGEN THERAPY (N=106)	NIV (N=110)	P-VALUE*
INTUBATION AT DAY 28 (% PATIENTS)				
Overall	47 (37 - 57)	38 (29 - 47)	50 (41 - 59)	0.18
Patients with PaO_2:FiO_2 ≤200 mmHg	53 (42 - 64)	35 (26 - 46)	58 (47 - 68)	0.009
VENTILATOR-FREE DAYS, n				
Overall	22±10	24±8	19±12	0.02
Patients with PaO_2:FiO_2 ≤200 mmHg	21±10	24±8	18±12	<0.001
MORTALITY, % PATIENTS				
In ICU	19 (12 - 28)	11 (6 - 9)	25 (17 - 33)	0.047
At 90 days	23 (16 - 33)	12 (7 - 20)	28 (21 - 37)	0.02

*For the three-group comparison.
Values are % patients (95% confidence intervals) or mean ± standard deviation.
FiO_2, fraction of inspired oxygen; ICU, intensive care unit; NHF, nasal high flow; NIV, noninvasive ventilation; PaO_2, partial pressure of arterial oxygen.

CONCLUSION:

There was no statistically significant difference between standard oxygen therapy, NHF oxygen therapy and NIV for the primary endpoint (intubation at 28 days). However, NHF oxygen therapy recipients with baseline PaO_2:FiO_2 ≤200 mmHg had a significantly lower 28-day intubation rate compared with the other two groups. In addition, all NHF oxygen therapy recipients had a significantly lower 90-day mortality rate.

KEY POINTS:

- There is no difference in the 28-day intubation rate in patients with acute hypoxemic respiratory failure treated with standard oxygen therapy, NHF oxygen therapy or NIV.
- Acute hypoxemic respiratory failure patients who have a baseline PaO_2:FiO_2 of ≤200 mmHg have a significantly lower 28-day intubation rate when treated with NHF oxygen therapy compared with standard oxygen therapy or NIV.
- In patients with acute hypoxemic respiratory failure, treatment with NHF oxygen therapy is associated with significant reduction in 90-day mortality compared with standard oxygen therapy or NIV.

Springer Healthcare Communications

STUDY 12 | **Stéphan F, Barrucand B, Petit P, Rézaiguia-Delclaux S, Médard A, Delannoy B et al.**
JAMA. 2015;313(23):2331-2339.

High-flow nasal oxygen vs noninvasive positive airway pressure in hypoxemic patients after cardiothoracic surgery. A randomized clinical trial.

AIM:

To investigate the noninferiority of nasal high-flow (NHF) oxygen therapy compared with bi-level positive airway pressure (BPAP) for preventing or resolving hypoxemic respiratory failure after cardiothoracic surgery.

METHOD:

This six-center, prospective, randomized, noninferiority trial included patients who had undergone cardiothoracic surgery and had met one of three criteria: failed a spontaneous breathing trial, had pre-existing risk factor(s) for postextubation acute respiratory failure, or had failed extubation after a successful spontaneous breathing trial. Patients were randomized in a 1:1 ratio to receive humidified NHF oxygen therapy (Optiflow™; Fisher & Paykel Healthcare) via a nasal cannula or BPAP via a full face mask delivered with either a ventilator specifically designed for BPAP (BiPAP® Vision®; Phillips Respironics) or an intensive care unit (ICU) ventilator with added positive end-expiratory pressure (PEEP, Dräger Evita® XL or 4; Dräger Medical SAS; or Monnal T75™; Air Liquide). Heat and moisture exchange filters were used during BPAP. The target oxygen saturation (SaO_2) for both arms was set at 92%–98%. The initial NHF flow rate was 50 L/min with an initial fraction of inspired oxygen (FiO_2) of 50%, which was then adjusted to maintain the target saturations. BPAP was initiated at 8 cmH_2O of pressure to achieve an exhaled tidal volume of 8 mL/kg and a respiratory rate of <25 breaths/minute. PEEP was initially set to 4 cmH_2O and FiO_2 of 0.5, and then adjusted to maintain the target SaO_2. BPAP was initially used for 2 hours, and then for ~1 hour every 4 hours or as needed to achieve clinical respiratory stability. Between sessions, patients in the BPAP group received standard oxygen therapy via standard nasal cannula to maintain SaO_2. Allocated treatment could be discontinued when SaO_2 was ≥95% at 6 L/min, PaO_2:FiO_2 ratio was ≥300 in NHF recipients, or when treatment was needed for <4 h/day in the BPAP group. Success was defined as absence of ventilatory support for 72 hours.

The primary endpoint was treatment failure (reintubation for mechanical ventilation, switch to other study treatment, or premature discontinuation of study treatment). Secondary outcomes included: ICU stay, changes in respiratory variables from baseline, at 1 hour, and 6–12 hours of treatment, dyspnea score, comfort score, skin breakdown score, and the rate of complications. *A priori*, the lower boundary of the 95% confidence interval was established as <9% in order for NHF oxygen therapy to be regarded as being noninferior to BPAP.

RESULTS:

A total of 830 patients were included in the study, 414 in the NHF group and 416 in the BPAP group. In both treatment groups, the most common form of cardiothoracic surgery was cardiopulmonary bypass (~80%).

NHF oxygen therapy was noninferior to BPAP for the primary study endpoint. This and other main study results are presented in the table. There were no significant differences between the NHF oxygen therapy and BPAP groups with respect to arterial carbon dioxide level ($PaCO_2$), pH, dyspnea score, comfort score, the number of nurse interventions per patient, ICU stay, or the rate of complications.

Stéphan F, Barrucand B, Petit P, Rézaiguia-Delclaux S, Médard A, Delannoy B et al.
JAMA. 2015;313(23):2331-2339.

VARIABLE	BIPAP (N=416)	NHF OXYGEN THERAPY (N=414)	RISK DIFFERENCE (%) (95% CI)
% Patients (95% CI)			
TREATMENT FAILURE			
Overall	21.9 (18.0 - 26.2)	21.0 (17.2 - 25.3)	0.9 (–4.9 - 6.6)[a]
Patients with PaO_2:FiO_2 ratio <200	24.8 (19.5 - 30.9)	27.5 (22.0 - 33.7)[b]	
Reintubation	13.7	14.0[c]	
Switch to other treatment	7.9 (5.6 - 11.0)	10.8 (8.5 - 14.9)[d]	
Premature discontinuation	3.6 (2.1 - 6.0)	1.4 (0.6 - 3.3)[e]	
ICU mortality	5.5 (3.6 - 8.3)	6.8 (4.6 - 9.7)[f]	
Secondary endpoints [mean (95% CI)]			
PaO_2:FiO_2			
Baseline	203 (195 - 212)	196 (187 - 204)	
1 hour	221 (213 - 230)[g]	184 (177 - 192)[hi]	
6–12 hours	261 (248 - 274)[j]	198 (187 - 208)[jk]	
RESPIRATORY RATE, BREATHS/MIN			
Baseline	23.3 (22.6 - 24.0)	22.8 (22.1 - 23.5)	
1 hour	23.0 (22.3 - 23.7)	21.0 (20.4 - 21.7)[gk]	
6–12 hours	22.5 (21.9 - 23.1)	21.6 (20.9 - 22.2)[l]	
FiO_2			
Baseline	0.47 (0.45 - 0.49)	0.49 (0.47 - 0.51)	
1 hour	0.55 (0.53 - 0.57)	0.60 (0.59 - 0.62)[k]	
6–12 hours	0.53 (0.51 - 0.56)	0.58 (0.57 - 0.60)[k]	

[a]p=0.003; [b]p=0.50; [c]p=0.99; [d]p=0.15; [e]p=0.04; [f]p=0.66; [g]p<0.001 vs baseline; [h]p=0.004 vs baseline; [i]p<0.01; [j]p<0.001 vs 1 hour; [k]p<0.001; [l]p=0.16
BPAP, bilevel positive airway pressure; CI, confidence interval; FiO_2, fraction of inspired oxygen; ICU, intensive care unit; NHF, nasal high flow; PaO_2, partial pressure of arterial oxygen.

CONCLUSION:

NHF oxygen therapy was noninferior to BPAP for the treatment of patients with, or at risk of, acute respiratory failure after cardiothoracic surgery.

KEY POINTS:

- In patients with, or at risk of, acute hypoxemic respiratory failure after cardiothoracic surgery, the rate of treatment failure in recipients of NHF oxygen therapy was noninferior to those treated with BPAP.
- NHF oxygen therapy appears to be an appropriate therapy for patients with, or at risk of, acute hypoxemic respiratory failure after cardiothoracic surgery.

Hernández G, Vaquero C, González P, Subira C, Frutos-Vivar F, Rialp G et al.
JAMA. 2016;315(13):1354-1361.

Effect of postextubation high-flow nasal cannula vs conventional oxygen therapy on reintubation in low-risk patients. A randomized clinical trial.

AIM:

To determine whether nasal high flow (NHF) oxygen therapy would reduce the need for reintubation compared with standard oxygen therapy when given immediately after planned extubation in mechanically ventilated patients at low risk for reintubation.

METHOD:

Patients receiving mechanical ventilation for >12 hours at seven intensive care units (ICUs) in Spain over the period September 2012 to October 2015 who passed a spontaneous breathing trial and were deemed at low risk for reintubation were eligible for inclusion in the study. Patients were randomized to receive NHF or standard oxygen therapy for the first 24 hours after extubation. NHF oxygen therapy (Optiflow™; Fisher & Paykel Healthcare) via a nasal cannula was initiated at a flow rate of 10 L/min, which was increased in 5 L/min increments; temperature was set to 37 °C unless this was too hot for the patient. Standard oxygen therapy was given via nasal cannula or nonrebreathing facemask. For both forms of oxygen therapy, the inspired oxygen fraction (FiO_2) was adjusted to maintain peripheral oxygen saturation (SpO_2) at >92%.

Demographic and clinical variables within the first 24 hours after admission were recorded. Arterial blood gases, Acute Physiology and Chronic Health Evaluation (APACHE) II score and use of steroids were determined at extubation. Variables recorded at 72 hours after extubation were extubation-related complications, nasal septum and skin trauma, reasons for intubation and time to reintubation. All patients were followed until hospital discharge, and total stay in the ICU and hospital was determined. In addition, patient status at discharge was noted.

The primary study endpoint was the rate of reintubation within 72 hours of extubation. Secondary endpoints included postextubation respiratory failure, respiratory infection, sepsis and multiorgan failure, length of stay and mortality in the ICU and hospital, reintubation and adverse events.

RESULTS:

Of the 1739 weanable patients who received mechanical ventilation for >12 hours over the study period, 527 were included and randomized to NHF (n=264) or standard (n=263) oxygen therapy (mean age 51.4 years, 62% male). Demographic and clinical characteristics were similar in the two treatment groups, apart from a lower incidence of neurologic comorbidities in the NHF (7.8%) versus standard (12.9%) oxygen therapy group.

No adverse events occurred during the study. The reintubation rate at 72 hours was 4.9% in the NHF group compared with 12.2% in the standard oxygen group (absolute difference 7.2%, 95% confidence interval [CI] 2.5 to 12.2%; p=0.004). This difference was largely due to a lower incidence of respiratory-related reintubations in the NHF versus standard oxygen therapy group (1.5% vs 8.7%; absolute difference 7.2%, 95% CI 3.6 to 11.4%; p=0.001). NHF oxygen therapy was independently and inversely associated with both all-cause (odds ratio [OR] 0.32, 95% CI 0.16 to 0.66) and respiratory-related (OR 0.17, 95% CI 0.06 to 0.51) reintubation. The number needed to treat with NHF oxygen therapy to prevent one reintubation was 14 (95% CI 8 to 40).

For secondary endpoints, the rate of post-extubation respiratory failure was significantly lower in the NHF group (8.3% vs 14.4% in the standard therapy group; difference 6.1%, 95% CI 0.7 to 11.6%; p=0.03). There were no statistically significant differences between the NHF and standard oxygen therapy groups with respect to median time to reintubation, respiratory infections, sepsis, organ failure, time to reintubation, length of stay in the ICU or hospital, and ICU or hospital mortality.

CONCLUSION:

Use of NHF oxygen therapy reduced the risk of reintubation within 72 hours compared with standard oxygen therapy in extubated patients at low risk for reintubation.

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Hernández G, Vaquero C, Colinas L, Cuena R, González P, Canabal A et al.
JAMA. 2016;316(15):1565.

Effect of postextubation high-flow nasal cannula vs noninvasive ventilation on reintubation and postextubation respiratory failure in high-risk patients: a randomized clinical trial.

AIM:

To investigate whether high-flow nasal cannula (HFNC) oxygen delivery immediately after planned extubation is noninferior to noninvasive ventilation (NIV) in the reduction of reintubation and postextubation respiratory failure in patients at high risk of extubation failure.

METHOD:

This was a randomized, multicenter study enrolling adults who had been on mechanical ventilation for >12 hours and were ready for scheduled extubation and considered at high risk of reintubation. High-risk patients met at least one of the following criteria: >65 years of age; heart failure is the primary indication for mechanical ventilation; moderate to severe chronic obstructive pulmonary disease; Acute Physiology and Chronic Health Evaluation II score >12 at extubation; body mass index >30 kg/m^2; impaired airway patency; inability to deal with respiratory secretions; difficult or prolonged weaning from mechanical ventilation; ≥2 comorbidities; and mechanical ventilation for >7 days. After completion of a spontaneous breathing trial, patients were randomly assigned to undergo HFNC or NIV for 24 hours immediately after extubation. Patients in the HFNC group received high-flow conditioned oxygen (Optiflow, Fisher & Paykel Healthcare) at an initial flow rate of 10 L/min, increased by 5 L/min until maximum tolerability was reached. The initial temperature was set at 37°C (unless reported as too hot), and the fraction of inspired oxygen (FiO_2) was adjusted to achieve a peripheral capillary oxygen saturation (SpO_2) >92%. After 24 hours, HFNC was discontinued and conventional oxygen therapy was administered as required. In the NIV group, patients underwent full face mask NIV (BiPAP Vision, Respironics Inc), with positive end-expiratory pressure (PEEP) and inspiratory pressure support adjusted to achieve a respiratory rate of 25 breaths/min and adequate gas exchange (arterial oxygen saturation [SaO_2] 92% and pH 7.35), and FiO_2 adjusted to maintain SpO_2 >92%. After 24 hours, NIV was stopped and patients received oxygen delivery by venturi mask. The primary outcomes were reintubation and postextubation respiratory failure within 72 hours of extubation; non-inferiority was established if the one-sided 95% confidence interval (CI) for the between-group difference was <10%. Secondary outcomes included reasons for failure of assigned treatment, respiratory infection, sepsis, multiple organ failure, intensive care unit (ICU) and hospital length of stay, and mortality.

RESULTS:

A total of 604 patients (mean age 65 years, 64% male) were randomized to receive HFNC (n=290) or NIV (n=314) after extubation. Baseline characteristics were similar in both groups, with the exception of a lower incidence of heart failure and a higher incidence of surgical diagnosis in the HFNC group. HFNC therapy was noninferior to NIV with regard to the rates of all-cause reintubation (between-group difference −3.7%; 95% CI −9.1 to ∞) and postextubation respiratory failure (between-group difference 12.9%; 95% CI 6.6 to ∞) within 72 hours of extubation (Figure 1). In addition, the rate of postextubation respiratory failure was lower in the HFNC than the NIV group. Respiratory-related reintubation (exploratory outcome) also occurred with similar incidences in the HFNC (16.9%) and NIV (15.9%) groups (between-group difference 1.0%; 95% CI −4.9 to 6.9). Within the first 7 days, one patient in the HFNC group required delayed reintubation for respiratory causes, and was included in the per-protocol analysis.

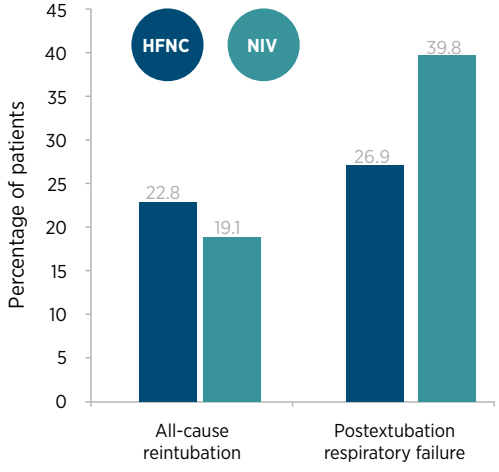

Figure 1. Primary outcomes within 72 hours of extubation among critically ill patients at high risk of extubation failure who received HFNC or NIV therapy.
HFNC, high-flow nasal cannula; NIV, noninvasive ventilation.

The causes for reintubation and postextubation respiratory failure (secondary outcomes) are summarized in Figure 2. Patients who required reintubation for persistent postextubation respiratory failure included those who were reintubated due to hypercapnia (2.1% [6/290] vs. 2.5% [8/314] in the HFNC and NIV groups, respectively). The non-respiratory causes in the HFNC and NIV groups included emergency surgery (0.7% vs. 1.3%) and a low level of consciousness (5.2% vs. 1.9%) [defined as a Glasgow Coma Scale score decrease >2 or total score <9 with partial pressure of carbon dioxide <45 mm Hg].

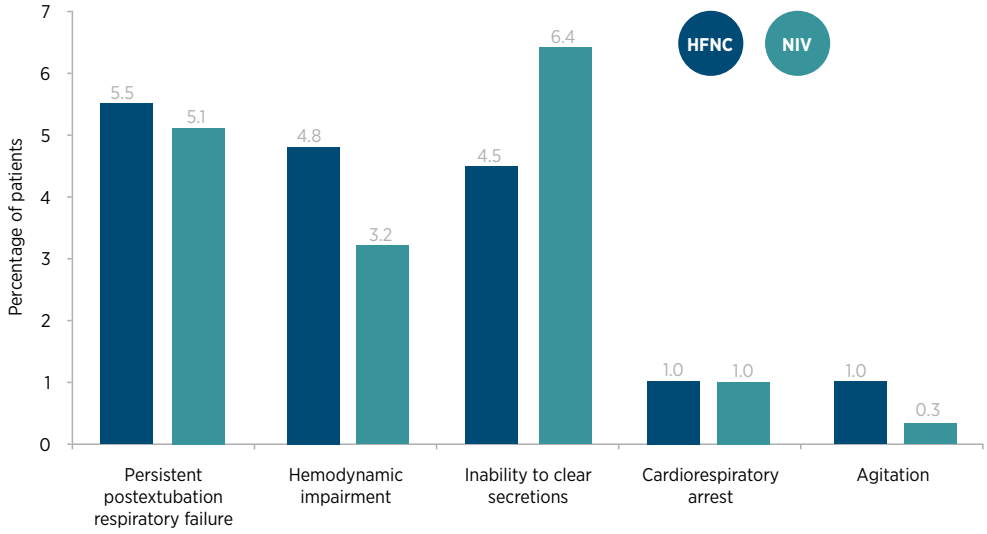

Figure 2 (A). Causes for reintubation within 72 hours of extubation among patients at high risk of extubation failure.

HFNC, high-flow nasal cannula; NIV, noninvasive ventilation.
**Glasgow Coma Scale score decrease >1 point.*

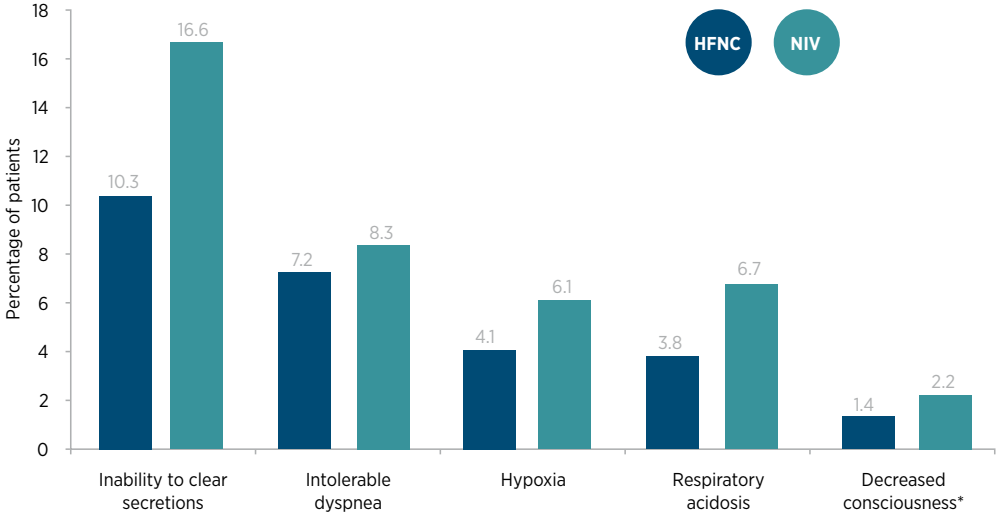

Figure 2 (B). Postextubation respiratory failure within 72 hours of extubation among patients at high risk of extubation failure.

HFNC, high-flow nasal cannula; NIV, noninvasive ventilation.
**Glasgow Coma Scale score decrease >1 point.*

Hernández G, Vaquero C, Colinas L, Cuena R, González P, Canabal A et al.
JAMA. 2016;316(15):1565.

Adverse events leading to treatment discontinuation for ≥6 hours of the per-protocol time occurred significantly more often in the NIV than the HFNC group (Figure 3). There were no reports of skin or nasal mucosa trauma in the HFNC group. The incidences of other secondary outcomes, including sepsis, multiple organ failure, respiratory infection (ventilator-associated tracheobronchitis or pneumonia), and ICU and hospital mortality, did not significantly differ between the treatment groups (Figure 3). The median length of ICU stay after randomization was significantly shorter in the HFNC than the NIV group (3 vs. 4 days; p = 0.048), although the median time to reintubation remained similar among patients on HFNC and NIV therapy (26.5 vs. 21.5 hours; between-group difference –5 hours; 95% CI –34 to 24).

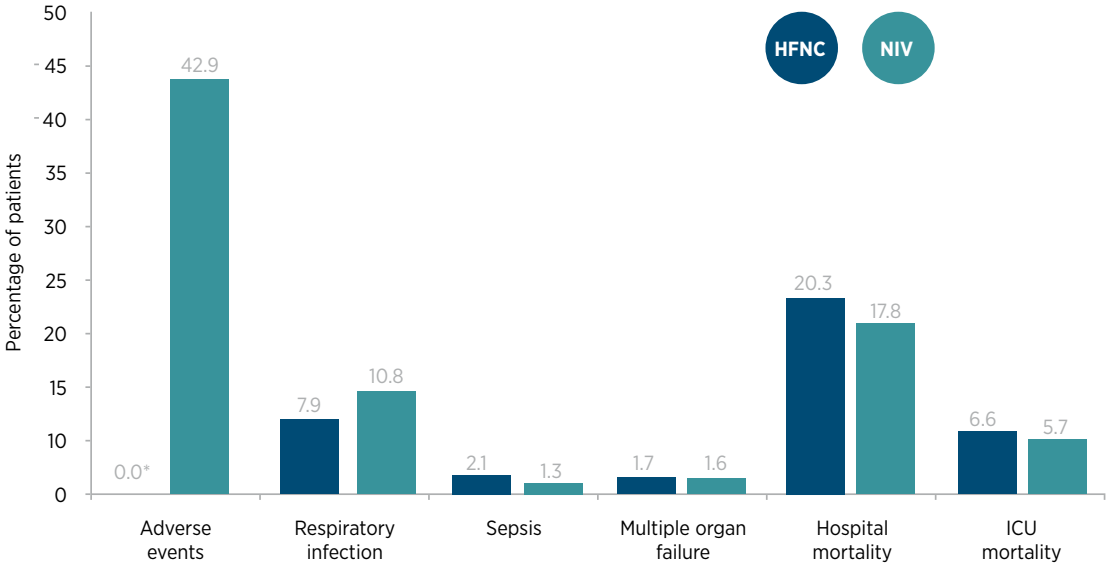

Figure 3. Incidence of adverse events requiring discontinuation for ≥18 hours and other secondary outcomes among patients at high risk of extubation failure. *p<0.001.

HFNC, high-flow nasal cannula; ICU, intensive care unit; NIV, noninvasive ventilation.

CONCLUSION:

The study indicated that postextubation HFNC is noninferior to NIV therapy for the prevention of reintubation and postextubation respiratory failure among adults at high risk for extubation failure.

KEY POINTS:

- HFNC is noninferior to NIV therapy as postextubation therapy for patients at high risk for extubation failure with regard to reintubation and postextubation respiratory failure within 72 hours of extubation.
- The incidence of postextubation respiratory failure within 72 hours of extubation was lower with HFNC than NIV therapy.
- The median length of ICU stay was significantly shorter with HFNC than NIV therapy.
- The incidence of adverse events requiring discontinuation for ≥18 hours was significantly lower with HFNC than NIV therapy.

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Nasal high flow oxygen therapy in the ward setting: a prospective observational study.

AIMS:

To evaluate the use of nasal high flow (NHF) oxygen therapy in hospitalized (ward) patients with respiratory failure or at risk of respiratory deterioration. To assess the timeliness of escalating treatment when NHF therapy fails.

METHODS:

Patient groups

Hospitalized adult patients (aged ≥ 18 years), with clinical signs of ongoing acute hypoxemia despite receiving conventional low-flow oxygen therapy, or who were at risk of respiratory deterioration as per clinicians' assessment

- All patients had the hospital patient at risk team (PART), or physiotherapists involved in their care.
- Oxygen saturation by pulse oximetry (SpO_2)/fraction of inspired oxygen (FiO_2) ratios were calculated to indicate the severity of their respiratory failure.
- Historically, severity of respiratory failure in the ICU has been assessed from the partial pressure of oxygen (PaO_2)/FiO_2 ratio; however, measurement of PaO_2 requires arterial blood gas measurement and is an uncomfortable procedure.

Study design

- Prospective observational study in tertiary metropolitan hospital in New Zealand

Primary outcome measure

Improvement in pulmonary function, as measured by:

- Decrease in respiratory and heart rate
- Increase in SpO_2

Secondary outcome measure

Improvements in dyspnea and sputum retention

Treatment regimens

NHF therapy (AIRVO™ 2 and Optiflow™; Fisher & Paykel Healthcare): median flow rate 30.0 L/min (q25, q75 = 30.00, 35.00), mean FiO_2 0.33 ± 0.10

RESULTS:

Enrolled patients

- Sixty-seven adult patients were enrolled between May and July 2015.
- Median age 71 years (q25, q75 = 58, 78); 61% male.
- The most common diagnosis contributing to respiratory failure was community-acquired pneumonia (incidence 29.9%), followed by hospital-acquired pneumonia (22.4%).
- After commencing NHF oxygen therapy, the mean SpO_2/FiO_2 ratio was 308.92 ± 87.41.

Primary endpoint

- After a median application time of 20 minutes, NHF therapy was associated with significant decreases from baseline in the respiratory rate (from 24.9 ± 5.9 to 23.7 ± 5.8; p = 0.007) and heart rate (from 93.9 ± 17.7 to 91.9 ± 18.2; p = 0.03), and an increase in SpO_2 (from 91.1 ± 4.8 to 93.4 ± 3.4; p < 0.001) [see table].
- Further improvements in the respiratory rate and SpO_2, but not the heart rate, were evident during the following 14 hours after commencing NHF
- These improvements were evident in patients prescribed NHF therapy by the PART team, but not in those prescribed by their physiotherapist.

Clinical efficacy of NHF therapy in hospitalized (ward) patients with respiratory failure or at risk of respiratory deterioration (data shown represent measures after 20 minutes of NHF therapy)

OUTCOME	BASELINE	AFTER 20 MINUTES NHF	STATISTICAL SIGNIFICANCE
Respiratory rate (mean)			
Total (n = 67)	24.97 ± 5.90	23.72 ± 5.84	t = 2.79, p = 0.007*, d = 0.21
PART (n = 30)	27.20 ± 4.92	25.47 ± 4.71	t = 2.49, p = 0.02*, d = -0.35
Physiotherapist (n = 27)	22.93 ± 6.25	21.93 ± 6.20	t = 1.51, p = 0.14
Heart rate (mean)			
Total (n = 67)	93.99 ± 17.71	91.90 ± 18.18	t = 2.23, p = 0.03*, d = 0.12
PART (n = 30)	98.20 ± 18.09	94.57 ± 18.67	t = 3.03, p = 0.005*, d = 0.20
Physiotherapist (n = 27)	89.93 ± 17.77	88.59 ± 18.96	t = 0.92, p = 0.37
SpO_2 (mean)			
Total (n = 67)	91.12 ± 4.82	93.39 ± 3.40	t = 4.08, p < 0.001*, d = -0.47
PART (n = 30)	90.40 ± 5.43	93.87 ± 3.06	t = 4.12, p < 0.001*, d = 0.60
Physiotherapist (n = 27)	91.96 ± 4.18	92.78 ± 3.91	t = 4.12, p = 0.21

t = parametric repeated measures t-test, d = Cohen's d

Secondary endpoint

- No improvement was seen in dyspnea or sputum retention after commencing NHF therapy

Other

- No delays in escalation of care were evident.
- Patients transferred to the ICU and/or (High dependency unit) HDU were on NHF therapy for shorter periods of time when compared to other patients.

KEY POINTS

- NHF therapy reduces ward patients' respiratory and heart rates and improves their oxygen saturation.
- Most ward patients receiving NHF therapy can be successfully managed in the ward setting and show clinical improvement.
- No delays in escalating care were found in the small number of ward patients receiving NHF therapy who were transferred to intensive or high dependency care.

Ischaki E, Pantazopoulos I, Zakynthinos S. Eur Respir Rev. 2017; Aug 9;26(145). Sep 30. [Epub ahead of print]. Used under Creative Commons license 4.0.

Nasal high flow therapy: a novel treatment rather than a more expensive oxygen device.

AIM:

To present available data on the physiological effects and clinical efficacy of nasal high flow (NHF) therapy across a range of clinical indications and propose an algorithm for the rational clinical application of NHF therapy in patients with acute hypoxemic respiratory failure (AHRF) of almost any cause.

METHOD:

Search criteria

- Trials and reviews of NHF therapy in adult patients in PubMed and the Cochrane Database
- Search limited to English-language publications using the terms "high flow" OR "heated" OR "humidified" AND "oxygen" OR "nasal oxygen" OR "nasal cannulae" in the text or title
- Last search conducted on April 1, 2017 (99 references are included)

RESULTS:

Mechanism of action overview

NHF therapy results in improved gas exchange, lower respiratory rate (RR) and effort, and improved lung volume, dynamic compliance, transpulmonary pressures, and homogeneity of ventilation

- Consequently, patients breathe more comfortably with less subjective dyspnea from the reduced work of breathing

Clinical implications overview

- The authors presented clinical data from studies across a range of indications in which NHF therapy has shown clinical benefit, including:
  - AHRF
  - Post-extubation in the ICU
  - Post-extubation following surgery
  - Pre- and peri-oxygenation during intubation
  - AHRF in immunocompromised patients
  - Studies in which NHF therapy had shown no clinical benefit were also presented for each of these indications
  - Other potential indications for NHF therapy (with very limited data) were also presented, including: during bronchoscopy; stable chronic obstructive pulmonary disease (COPD) with chronic respiratory failure; decompensated heart failure; and in patients who have the status "do not intubate"

An algorithm for clinical use

- Based on the existing literature on NHF therapy in patients with AHRF, the authors proposed an algorithm for use when NHF therapy is available and has been chosen as the initial oxygen delivery device (shown below)

In summary:

- If a patient is admitted with clinical signs of acute respiratory distress and blood gas analysis demonstrates hypoxemia (PaO_2/FiO_2 < 300) of almost any cause without hypercapnia ($PaCO_2$ > 45 mmHg with pH < 7.35), check primarily whether or not the criteria for imminent intubation and invasive mechanical ventilation are met (see algorithm)
  - If the criteria are met, intubation should be performed (NHF may be used for pre-oxygenation and apneic oxygenation during laryngoscopy)
  - If the criteria are not met, NHF should be initiated as soon as possible
- Monitoring for respiratory parameters with negative prognostic significance should be performed within 1 to 2 hours of NHF initiation
  - This allows for early identification of patients not responding to NHF therapy. (They could be considered for a short course of noninvasive ventilation [NIV] prior to intubating)
  - NHF settings should be checked and adjusted accordingly during the monitoring of the patient

- Flow rate could be adjusted downwards by 5 to 10 L/min every 1 to 2 hours if no negative prognostic factors are present
- If targets of SpO_2 and RR are not achieved while the flow rate is < 60 L/min, the flow rate can be increased by 5 to 10 L/min rather than raising the FiO_2. (Higher flow rates reduce entrainment of room air during inspiration and increase the airway pressure linearly, thus recruiting more alveolar units)
- If SpO_2 remains low, then an increase in FiO_2 is required

- Patients under NHF therapy should be monitored closely to avoid undesired respiratory and cardiac complications with a maximum timeframe of 48 hours
  - Parameters that require regular monitoring include respiratory parameters and those which indicate hemodynamic instability
- If no improvement in seen within 48 hours, NHF therapy should be considered to have failed and intubation and mechanical ventilation should be initiated as soon as possible. (Maintaining a failed NHF therapy could disguise further respiratory deterioration and increase mortality)
- If clinical and gasometric parameters gradually improve, then weaning from NHF can be commenced
  - FiO_2 should first be lowered to 40 to 50%, proceeding with a stepped decrease in flow rate of 5 to 10 L/min. (The intervals of these decrements can be longer or shorter depending on the patient's clinical and physiological parameters)
  - When the patient is stable for 1 to 2 hours with FiO_2 at 40% and flow rate at < 15 L/min, NHF should be stopped and a Venturi mask or nasal oxygen can be commenced

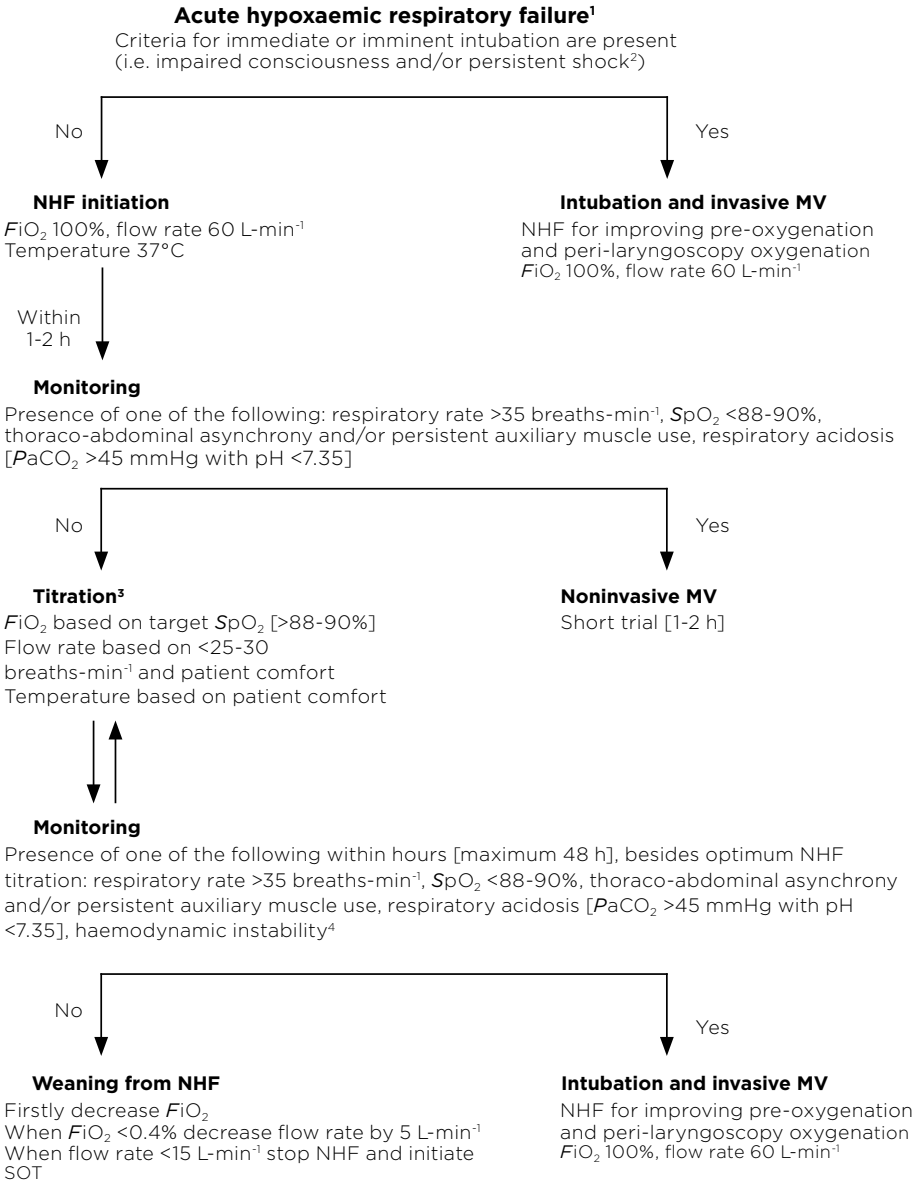
CONCLUSIONS:

Mechanism of action overview

- More stable FiO_2, CO_2 wash-out effect, PAP generation, and effective hydration of the administered gas are the main mechanisms behind the greater perceived comfort and tolerance of NHF therapy by the patient, as well as more effective oxygenation and improved breathing with less dyspnea
- Further controlled studies are needed in specific diseases and types of respiratory failure to determine which types of patients will benefit most from NHF therapy
  - Special attention should be given to the settings of FiO_2 and flow rate per disease and the maximum safe duration of NHF application before the initiation of NIV or invasive mechanical ventilation
  - Currently, the choice of supplemental oxygen should be personalized and based on a patient's clinical status, underlying disease, severity of hypoxemia, coexistence of hypercapnia, and their level of tolerance and comfort

KEY POINTS:

- The beneficial effects of NHF therapy over standard oxygen therapy are reported in most of the studies identified in this review
- An algorithm is proposed for cases of NHF application in patients with AHRF of almost any cause
- The choice of supplemental oxygen therapy should be personalized, and based on the patient's clinical status, underlying disease, severity of hypoxemia, coexistence of hypercapnia, and their level of tolerance and comfort



1 Recommended algorithm for nasal high flow use in acute hypoxaemic respiratory failure in immunocompetent of immunocompromised patients, those with PaO_2/FiO_2 < 300. Those with $PaCO_2$ > 45mmHg and pH < 7.35 are excluded.

2 Systolic arterial blood pressure < 90 mmHg despite adequate fluid administration.

3 The rationale for change in NHF settings:

a) Flow rate could be reduced by 5-10 L/min^{-1} per 1-2h if none of the negative prognostic factors are present. However, if targets of arterial oxygen saturation measured by pulse oximetry (SpO_2) and respiratory rate are not achieved, while the flow rate is still < 60 L/min^{-1}, increase of flow rate by 5-10 L/min^{-1} is preferred to raising FiO_2.

b) Increase in FiO_2 causes increase in PaO_2 and SpO_2.

c) Temperature can be set at 37 °C or lower (31-34 °C), based on the patient's comfort.

4 Hemodynamic instability is defined by heart rate > 140 beats/min-1 or change > 20% from baseline and/or systolic arterial blood pressure > 180 mmHg, < 90 mmHg or decrease > 40 mmHg from baseline.

MV = mechanical ventilation; SOT = standard oxygen treatment

Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G, et al.
Am J Respir Crit Care Med. 2018 Dec 21.

An index combining respiratory rate and oxygenation to predict outcome of nasal high flow therapy.

AIM:

To validate the prognostic accuracy of an index (termed ROX) for determining nasal high flow cannula (NHF) therapy outcomes.

METHOD:

Patient group

- Patients with pneumonia and acute hypoxemic respiratory failure (AHRF) treated with NHF in five ICUs across Spain and France
- Exclusion criteria were: patients < 18 years, those with an indication for immediate intubation, and those with a 'do not intubate' order
- Patients were followed until death or hospital discharge

Study design

- Two-year multicenter prospective observational cohort study

Outcome

Association of ROX index with NHF outcome

- Determined through Cox proportional hazards modeling
- ROX index was defined as the ratio of oxygen saturation [SpO_2]/fraction of inspired oxygen [FiO_2] to respiratory rate. Variables with a positive association with NHF success were in the numerator field, and variables with an inverse relation to NHF success were in the denominator field

Treatment regimen

High flow was provided with the Optiflow™ device (MR850 heated humidified delivery tubing and nasal cannula, Fisher & Paykel Healthcare) or with Airvo™ 2 (Fisher & Paykel Healthcare)

- NHF was initiated with a minimum flow of 30 L/min with an FiO_2 = 1 in those patients that were unable to maintain an SpO_2 > 92% and a respiratory rate ≥ 25 breaths/min while receiving standard oxygen administered through a face mask at ≥ 10 L/min
- FiO_2 was then titrated targeting an SpO_2 > 92%, and the flow rate was adjusted according to the maximum tolerated rate
- In all patients, the maximum tolerated flow was achieved within the first 10 minutes of NHF treatment

RESULTS:

'Intent-to-treat' group

191 and 157 patients were treated with NHF in the validation and training cohorts, respectively

- Results regarding the training cohort are reported elsewhere (Roca et al. J Crit Care 2016)

Results

Of 191 patients treated with NHF in the validation cohort, 68 (35.6%) required intubation and mechanical ventilation

- The median duration of NHF therapy in success and failure patient groups was 96 (48 to 144) hours and 24 (12 to 60) hours, respectively (P < 0.001)

Patients with NHF success had a higher SpO_2/FiO_2 and a lower respiratory rate after NHF and throughout the study period (see the table below)

- Higher ROX index values were observed in those patients who had success with NHF

The prediction accuracy of the ROX index increased over time (area under ROC curve at 2 h 0.679; 6 h 0.703; 12 h 0.759)

- ROX ≥ 4.88 measured at 2 hours (HR 0.434 [95% CI 0.264 to 0.715]; p = 0.001), 6 hours (HR 0.304 [95% CI, 0.182 to 0.509]; p < 0.001), or 12 hours (HR 0.291 [95% CI 0.161 to 0.524]; p < 0.001) after NHF initiation was consistently associated with a lower risk of intubation

ROX values < 2.85, < 3.47, and < 3.85 at 2, 6, and 12 hours, respectively, after NHF initiation were predictors of NHF failure

- Patients with NHF failure presented a lower increase in the values of the ROX index over 12 hours

Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G, et al.
Am J Respir Crit Care Med. 2018 Dec 21.

VARIABLE	TIME	SUCCESS (n = 123)	FAILURE (n = 68)	P VALUE
SpO_2/FiO_2	Prior to NHF	180	106	0.005
	2h	155	109	0.003
	6h	160	115	0.001
	12h	165	113	0.001
	18h	176	118	0.002
	24h	194	120	<0.001
Respiratory rate (bpm)	Prior to NHF	28	32	0.778
	2h	25	28	0.023
	6h	24	26	0.003
	12h	23	26	<0.001
	18h	22	25	0.001
	24h	21	24	0.004
ROX index	Prior to NHF	5.81	4.06	0.169
	2h	5.71	4.43	0.001
	6h	6.55	4.86	<0.001
	12h	7.53	4.78	<0.001
	18h	8.60	5.10	<0.001
	24h	8.68	5.05	<0.001

CONCLUSIONS AND KEY POINTS:

- The results indicate that the ROX index can help to predict the outcomes of NHF therapy in patients with AHRF due to pneumonia
- Dynamic changes in its value may help to identify those patients who will succeed with NHF and those who will fail
- Among measured components, the SpO_2/FiO_2 had a greater predictive weight than the respiratory rate
- The index can be measured with ease and repetition at the bedside, thereby facilitating day-to-day clinical decision-making for critically ill patients treated with NHF

Effect of post-extubation high-flow nasal oxygen with noninvasive ventilation vs high-flow nasal oxygen alone on reintubation among patients at high risk of extubation failure: a randomized clinical trial.

AIM:

To determine whether nasal high flow (NHF) oxygen with prophylactic noninvasive ventilation (NIV), applied immediately after extubation, could reduce the rate of re-intubation compared with NHF alone in patients at high risk of extubation failure in the intensive care unit (ICU).

METHOD:

Patient group

Adult patients intubated for > 24 hours in the ICU and ready for extubation were enrolled if they were at high risk of extubation failure (> 65 years or with an underlying cardiac or respiratory disease).

- Patients were included from 30 ICUs in France.
- Underlying chronic cardiac diseases included left ventricular dysfunction (defined by left ventricular ejection fraction ≤ 45%); history of cardiogenic pulmonary edema; documented ischemic heart disease; or permanent atrial fibrillation.
- Underlying chronic lung diseases included chronic obstructive pulmonary disease, obesity-hypoventilation syndrome, or restrictive pulmonary disease.

Study design

A multi-center randomized clinical trial conducted from April 2017 to January 2018

- Follow-up until April 2018

Primary outcome

The primary outcome was the proportion of patients re-intubated at day 7 following extubation.

- Patients were immediately re-intubated if one of the following criteria was met: severe respiratory failure, hemodynamic failure with the need for vasopressors, neurological failure (altered consciousness with a Glasgow Coma Scale score < 12), or cardiac or respiratory arrest.

Secondary outcomes

- Secondary outcomes included postextubation respiratory failure at day 7, re-intubation rates up until ICU discharge, and ICU mortality.

Treatment regimen

- Patients were randomly assigned to NHF alone (control, n = 306) or NHF/NIV (n = 342) immediately after extubation.
- Patients in the control group were continuously treated with NHF alone for ≥ 48 hours at a flow rate of 50 L/min and fraction of inspired oxygen (FiO_2) adjusted to obtain adequate oxygenation, with an oxygen saturation by pulse oximetry (SpO_2) of ≥ 92%.
- In patients assigned to NHF/NIV, NHF was delivered as in the control group; NIV was initiated immediately after extubation with a first session of ≥ 4 hours and minimal duration of ≥ 12 hours/day during the 48 hours following extubation.
- NIV was carried out with a minimal pressure-support level of 5 cmH_2O targeting a tidal volume 6 to 8 mL/kg of predicted body weight, a positive end-expiratory pressure level between 5 and 10 cmH_2O, and a FiO_2 adjusted to obtain adequate oxygenation (SpO_2 ≥ 92%).
- Blood gases were performed 1 hour after treatment initiation, and patients were treated for a minimum of 48 hours.
- When there were no signs of respiratory failure 48 hours after extubation, treatment was stopped and switched to standard oxygen.

RESULTS:

Intent to treat group

Among 648 patients who were randomized (mean [± SD] age, 70 [± 10] years; 34% female), 641 completed the trial.

- Patient characteristics at inclusion were similar between treatment groups except for a higher proportion of patients with underlying chronic lung disease in the NIV group.
- The median duration of mechanical ventilation prior to extubation was 5 days (interquartile range [IQR], 3 to 10 days).
- Initial mean (± SD) settings in the NHF alone group were: gas flow rate 50 (± 5) L/min with FiO_2 of 0.41 (± 0.13).
- Initial mean (± SD) settings in the NHF/NIV group were: pressure-support level 7.8 (± 2.5) cmH_2O, positive end-expiratory pressure 5.3 (± 1.1) cmH_2O, and FiO_2 0.34 (± 0.10), resulting in a tidal volume of 8.6 (± 2.9) mL/kg of predicted body weight.
- NIV was delivered for a mean (± SD) of 22 (± 9) hours within the first 48 hours following extubation (mean 13 hours within the first 24 hours) and was delivered for ≤ 4 hours due to intolerance in 20 patients (± 6%).

Primary outcome

The re-intubation rate at day 7 was 11.8% (95% confidence interval [CI], 8.4 to 15.2%) with NHF/NIV vs. 18.2% (95% CI, 13.9 to 22.6%) with NHF alone.

- The difference was −6.4% (95% CI, −12.0 to −0.9%; P = 0.02).

Secondary outcomes

Among the 11 prespecified secondary outcomes, 6 showed no significant difference.

- The proportion of patients with postextubation respiratory failure at day 7 (21% vs. 29%; difference, −8.7% [95% CI, −15.2 to −1.8%]; P = 0.01) and re-intubation rates up until ICU discharge (12 vs. 20%, difference −7.4% [95% CI, −13.2 to −1.8%]; P = 0.009) were significantly lower with NHF/NIV than with NHF alone.
- NIV was continued beyond the first 48 hours for incomplete recovery of respiratory status in 86 patients (25%) in the NHF/NIV group; in the NHF group, NHF was continued in 106 patients (35%) (difference, −9.7% [95% CI, −16.8 to −2.6%]; P < 0.01).
- Mortality in the ICU, in the hospital, and at day 90 were not significantly different between groups: 6% with NHF/NIV and 9% with NHF alone (difference, −2.4% [95% CI, −6.7 to 1.7%]; P = 0.25).
- No severe adverse events attributable to treatment were observed during the study.

CONCLUSIONS AND KEY POINTS:

In mechanically ventilated patients at high risk of extubation failure, the use of NHF with NIV (immediately after extubation) significantly decreased the risk of re-intubation within the first seven days compared with NHF alone.

Bräunlich, J., Köhler, M. and Wirtz, H.
International Journal of Chronic Obstructive Pulmonary Disease. 2016;1077-1085.

Nasal high flow improves ventilation in patients with COPD.

AIM:

To investigate the effects of nasal high flow (NHF) rate on ventilatory parameters, clinical benefits, and hypercapnia in patients with chronic obstructive pulmonary disease (COPD). NHF was also compared with nasal bilevel positive airway pressure (nBiPAP) and nasal continuous positive airway pressure (nCPAP) to elucidate the NHF mechanism of action.

METHOD:

The TNI softFlow 50 device (TNI medical AG) was used to apply NHF with nasal prongs with different bore outlets (small, medium and large). The nasal BiPAP and nCPAP were applied using a nose mask (BiPAP Synchrony; Philips Respironics). A total of 67 hospitalized patients with COPD (GOLD class C/D), in stable condition and without acute exacerbation or right heart decompensation were recruited from the respiratory ward at the University Hospital of Leipzig from April 2015 to December 2015. Patients were allocated to one or more of three groups: group A for measurement of airway pressure; group B for measurements of tidal volume (VT), breathing rate (BR) and minute ventilation; or group C, provided they had chronic ventilatory insufficiency and hypercapnia, for blood gas analysis.

Group A patients were consecutively required to use the NHF device with flow rates of 10 L/min, 20 L/min, 30 L/min, 40 L/min and 50 L/min, followed by nCPAP and nBiPAP. The airway pressure was measured with patients in a sitting position using a water-filled flexible tube as a pressure transducer (Original Perfusor®-cable; B. Braun) placed in the nasopharyngeal space; the signal was then measured by a pressure sensor (GMH3111, Greisinger Electronic GmBH). Ten breaths were recorded during spontaneous breathing (baseline), nCPAP/nBiPAP breathing, and NHF breathing.

BR, VT and MV were measured with group B patients in a sitting position by placing elastic sensor belts 10 cm below the jugular notch and 10 cm below the xiphoid process, and data were recorded using a polysomnograph (Respitrace; CareFusion GmbH, Höchberg, Germany). The device was calibrated for each patient using standard lung function equipment (Master Screen Body; CareFusion GmbH). Volume measurements during NHF and spontaneous breathing were carried out, chest and abdominal excursions were recorded. Work of breathing was expressed as rapid shallow breathing index (RSBI; breaths per min/VT [L]).

Measurements of capillary blood gases from the earlobe were performed on group C patients under constant oxygen supplementation before and 2 hours after NHF breathing.

Patient satisfaction was evaluated using a comfort scale (range: 1, more comfortable; 10, less comfortable) and a dyspnea scale (range: 1, less dyspnea; 5, more dyspnea).

Bräunlich, J., Köhler, M. and Wirtz, H.
International Journal of Chronic Obstructive Pulmonary Disease. 2016;1077-1085.

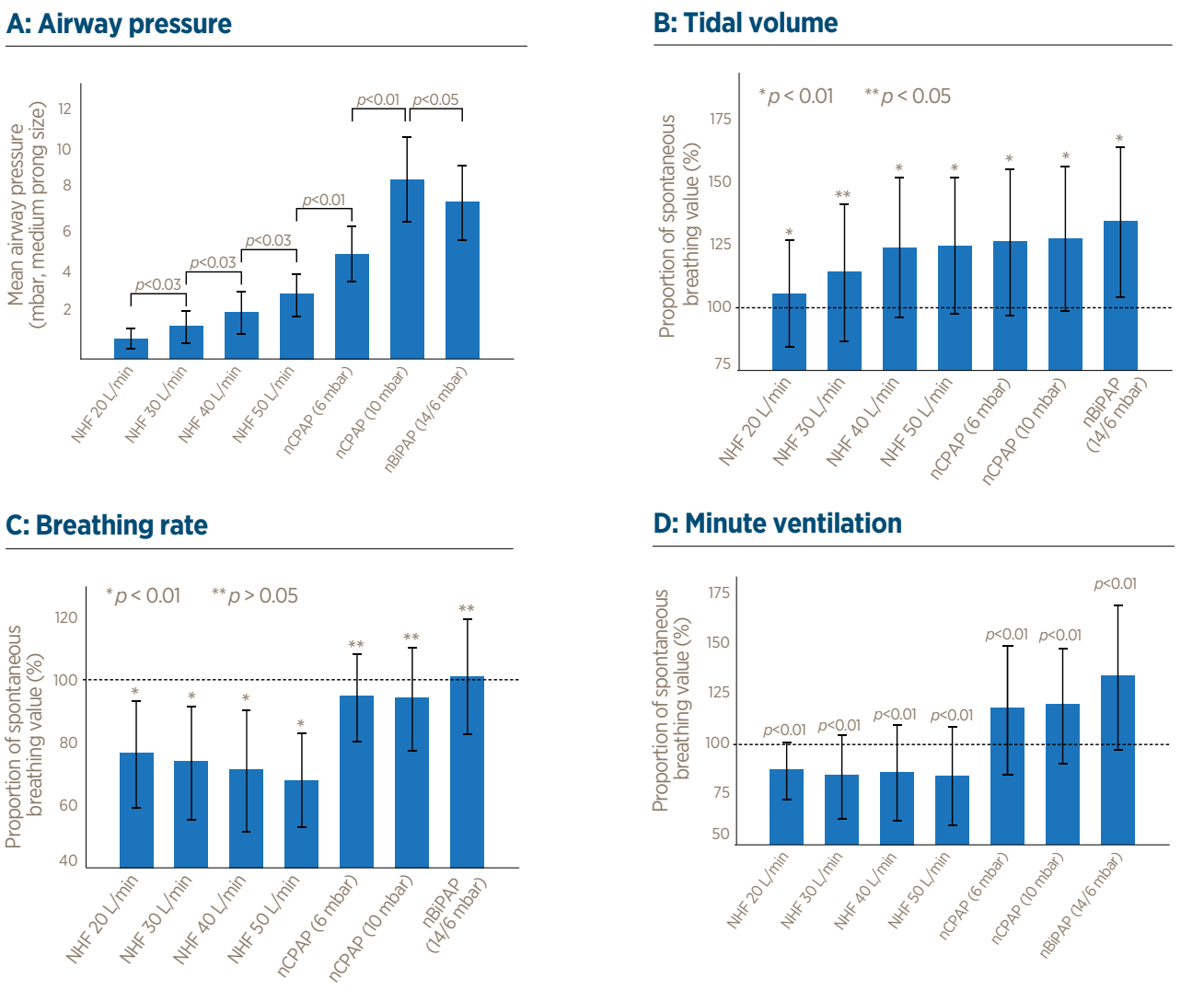


Figure 1. A, mean airway pressure (p-value refers to comparison with previous applied device); B-D, proportion of spontaneous breathing value (p-values in comparison with spontaneous breathing) for B, tidal volume; C, breathing rate; D, minute ventilation. NHF, nasal high flow using medium prongs; nBiPAP, nasal bilevel positive airway pressure; nCPAP, nasal continuous positive airway pressure.

RESULTS:

Groups A (n = 19), B (n = 18) and C (n = 54) had similar baseline characteristics, with the exception of a lower predicted forced vital capacity, a higher predicted total airway resistance, and higher capillary pCO_2 in group C. Key results are presented in Figure 1. During NHF breathing, a flow-dependent increase in mean airway pressure was recorded, which was not affected by prong size (Fig. 1A). nCPAP and nBiPAP also led to an increase in mean airway pressure (Fig. 1A).

All ventilation support devices significantly increased VT compared with spontaneous breathing, independently of flow rate, prong size, device, or pressure settings (Fig. 1B). BR decreased significantly as NHF rate increased, although the correlation was not statistically significant and prong size did not affect BR (Fig. 1C). nCPAP and nBiPAP did not influence BR (Fig. 1C). Whilst minute ventilation was decreased by NHF, it was increased by nCPAP and nBiPAP (Fig. 1D). Inspiration/expiration ratio was not altered by any of

the ventilatory support devices. All the ventilatory support devices significantly decreased RSBI in all groups with similar magnitude, although increasing NHF rate seemed to enhance this effect. NHF breathing led to a significant decrease in hypercapnia, which augmented as NHF flow increased (91.0% [p<0.01] and 87.4% [p<0.01] of the baseline pCO_2 value with 20 L/min and 30 L/min, p<0.03 between the two flow rates). This also resulted in a pH increase, which was not affected by flow rate. No changes in pO_2 between baseline and between different flows were recorded. Of all the devices, NHF was rated as the most comfortable with the least dyspnea by patients.

DISCUSSION:

NHF, nCPAP and nBiPAP all led to a decreased RSBI, a measure of the work of breathing in patients with COPD. In patients supported by nCPAP or nBiPAP, the VT increased whilst the breathing rate remained constant, resulting in an increased minute ventilation. However, in patients supported by NHF, whilst the tidal volume increased, the breathing rate decreased and therefore the minute ventilation decreased. Despite the decreased minute ventilation, NHF demonstrated a reduction in hypercapnia. As flow increased for NHF and nCPAP, airway pressure increased, although it remained lower for NHF than for nCPAP and nBiPAP. Higher air flow may facilitate the replacement of exhaled air, high in pCO_2, with fresh air, low in pCO_2, thereby reducing the amount of exhaled gas that is rebreathed. In patients using the NHF device, this washout hypothesis could explain how reduced hypercapnia was achieved despite a lower minute ventilation. Furthermore, NHF was the patients' preferred ventilation device in terms of comfort and reduction of dyspnea.

CONCLUSION:

NHF improves breathing patterns in patients with hypercapnic COPD; it decreases the work of breathing and consequently reduces pCO_2 levels as observed with nCPAP and nBiPAP but the most likely mechanism is through reduction of dead space and washout.

KEY POINTS:

- NHF reduces the work of breathing and pCO_2, thereby enhancing effectiveness of breathing in patients with COPD and hypercapnia.
- NHF ventilation support leads to a flow-dependent reduction in pCO_2 in patients with COPD and hypercapnia.
- Higher air flow is likely to cause a washout of the respiratory tract, replacing high-pCO_2 exhaled air with low-pCO_2 fresh air, thereby reducing hypercapnia.
- Overall, patients felt NHF was more comfortable and better at reducing dyspnea than nCPAP or nBiPAP.

STUDY 20 | **Hasani A, Chapman T, McCool D, Smith R, Dilworth J, Agnew J.**
Chron Respir Dis. 2008;5(2):81-86.

Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis.

AIM:

To determine the effects of heated humidification therapy on mucociliary clearance in patients with bronchiectasis.

METHOD:

Fourteen subjects with bronchiectasis confirmed by high resolution computed tomography entered the study. Four withdrew during the screening phase; leaving ten patients for treatment and analysis (mean age 63 years).

Humidification therapy was provided by an MR880 heated humidifier (Fisher & Paykel Healthcare). The system provided air at 37 °C and fully saturated with water vapour (100% relative humidity) via nasal cannula at a flow rate of 20-25 L/min. Patients were instructed to use humidification therapy for 3 hours as an acute treatment, then for 3 hours each day for 6 days as a short term treatment. Patient compliance was recorded automatically as patients used the system (usage time of the blower supplying the humidifier with air was recorded). Assessments were performed at baseline and after treatment; these included lung function (assessed by a spirometer) and tracheobronchial clearance as a measure of mucociliary clearance assessed using a radioaerosol technique.

RESULTS:

Nine out of ten patients used humidification for longer than the target study treatment duration of 21 hours; median duration of humidification was 25.0 hours (range 14.9 to 26.9). All patients successfully used the humidification system and rated it as very acceptable. Tracheobronchial clearance (mucociliary clearance) was significantly improved by humidification therapy, as shown by significant improvements in radio-aerosol movement. There was a nonsignificant reduction in the number of coughs after short-term humidification therapy, and lung function parameters also tended to improve compared with baseline.

DISCUSSION:

Mucociliary clearance is the first-line defense mechanism in the upper and lower airways. Patients with bronchiectasis have lung mucous retention and experience a high rate of respiratory infection. Effective mucociliary clearance has been shown to be dependent on sufficient airway surface liquid volume. The improvement in mucociliary clearance seen in this study after heated humidification therapy in patients with bronchiectasis for three hours per day has the potential to decrease the risk of respiratory infection and disease exacerbations, and thus slow the rate of disease progression. Further studies are required to see whether the short-term benefits observed in this study persist during longer term therapy.

CONCLUSION:

Humidification therapy appears to have a protective effect in patients with bronchiectasis by improving mucociliary clearance.

KEY POINTS:

- Providing inspired air at 37 °C and fully saturated with water vapour (100% relative humidity) via nasal cannula at a flow rate of 20-25 L/min for three hours per day significantly improves mucociliary clearance in patients with bronchiectasis.
- Improved mucociliary clearance in patients with bronchiectasis has the potential to decrease the rate of respiratory infections and may therefore slow the rate of disease progression.

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Mündel T, Feng S, Tatkov S, Schneider H.
J Appl Physiol. 2013;114(8):1058-1065.

Mechanisms of nasal high flow on ventilation during wakefulness and sleep.

AIM:

To evaluate the effects of nasal high flow (NHF) on respiratory responses during wakefulness and sleep in healthy volunteers. The pressure/air-flow relationships of NHF and continuous positive airway pressure (CPAP) were also compared using a nasal cavity model.

METHOD:

This randomized, crossover trial included healthy participants without sleep abnormalities. The study was conducted when participants were either in a state of wakefulness or sleep. During wakefulness, participants were randomized to one of four arms (NHF at flow rates of 15, 30, or 45 L/min, or no NHF [control]). During sleep, subjects were randomized to one of three arms (NHF at flow rates of 15 or 30 L/min, or no NHF [control]).

Participants were treated with NHF using a high-flow humidification system (AIRVO™; Fisher & Paykel Healthcare), which delivered air at 37 °C that was fully saturated with water via a nasal cannula (Optiflow™ OPT844 Medium; Fisher & Paykel Healthcare). Outcomes that were assessed included changes in respiratory rate, tidal volume, and minute ventilation.

A nasal cavity model was also used to investigate the pressure/air-flow relationships over the range of inspiratory and expiratory phases following the use of NHF (OPT844 and OPT846) or nasal mask CPAP (HC600; Fisher & Paykel Healthcare, New Zealand).

RESULTS:

A total of 10 healthy participants (mean ± standard deviation age 22 ± 1.3 years) were included in the study. During wakefulness, tidal volumes were significantly increased from baseline at flow rates of 15 ($p<0.005$), 30 ($p<0.05$), and 45 ($p<0.005$) L/min. In contrast, respiratory rates were significantly reduced from baseline with all NHF interventions ($p<0.001$, $p<0.005$, and $p<0.005$, respectively). No significant changes in tidal volume or respiratory rate were seen in controls. The decrease in respiratory rate was mainly due to significant increases in expiratory times, from 3.1 ± 0.8 sec with controls to 4.9 ± 1.5 sec with NHF at 30 L/min ($p<0.01$), and 6.0 ± 2.3 sec with NHF at 45 L/min ($p<0.001$). The increase in tidal volumes and decrease in respiratory rates led to a small increase in minute ventilation.

During sleep, NHF was associated with a reduction in tidal volume and no change in respiratory rate. This in turn resulted in a decrease of approximately 20% in minute ventilation.

In the nasal cavity model, NHF at a flow rate of 15 L/min increased resistance during expiration and decreased resistance during inspiration. These changes in resistance were dependent on the expiratory flow rate and the cannula size. In contrast, nasal mask CPAP did not change inspiratory or expiratory resistance. Furthermore, a greater increase in expiratory pressure was seen with NHF.

CONCLUSION:

The results of this study indicate that there are marked differences in respiratory responses to NHF during states of wakefulness and sleep in healthy volunteers. Furthermore, the mechanical effects of NHF (increased expiratory and decreased inspiratory resistance) on the upper airways appear to be different from that of CPAP. These findings suggest that NHF may be an effective option for improving tidal breathing during wakefulness in patients with respiratory or cardiac dysfunction, and may also be used to relieve respiratory loads during sleep.

KEY POINTS:

- Breathing patterns are sleep/wake dependent: during wakefulness NHF increases tidal volume and decreases respiration rate; during sleep NHF reduces ventilation by decreasing tidal volume while maintaining respiratory rate.
- NHF reduces the proportion of dead space volume breathing.
- In a nasal cavity model, NHF increases expiratory and decreases inspiratory resistance; no such changes are seen with CPAP.
- NHF may be an effective option for the management of patients with cardiorespiratory diseases.

inScience Communications

STUDY 22 | **Parke R, McGuinness S, Eccleston M.**
British Journal of Anaesthesia. 2009;103(6):886-890.

Nasal high-flow therapy delivers low level positive airway pressure.

AIM:

To compare the level of positive airway pressure generated by a new respiratory support therapy, Nasal High Flow (NHF) using the Optiflow™ system, with that of a traditional facemask.

METHOD:

A 10F catheter was inserted into the nasopharynx of adults who had undergone elective cardiothoracic surgery; all patients were in the cardiothoracic ICU and were still sedated and ventilated at the time of catheter insertion. The next day, following extubation, patients received respiratory support with a heated and humidified oxygen/air blend delivered using the Optiflow™ system (MR880 Heated Humidifier plus RT241 heated delivery tube; Fisher & Paykel Healthcare) with either the Optiflow™ wide-bore nasal cannula (NHF) or a traditional facemask as the patient interface. Nasopharyngeal airway pressure was measured using a pressure transducer connected to the previously placed catheter, as the most reasonable surrogate for transpulmonary pressure.

Humidified oxygen therapy (target 37 °C, Absolute Humidity 44 mg H_2O) at 35 L/min was administered for approximately 15 minutes using the Optiflow™ system to allow patients to acclimatize their breathing patterns. Airway pressure was then measured during 1 minute of quiet breathing, and then repeated after the interface was changed to a standard facemask (Medium Adult SEE-THRU® O_2 Mask; Hudson Respiratory Care Inc.).

Measurements were recorded with mouth open and closed, and a washout period of 5 minutes was allowed between each trial.

RESULTS:

19 patients (17 men and 2 women, mean age 63 years) were recruited into the study, and data from 15 were analysed – 4 were excluded because they returned from theatre in a critical condition, or the catheter was dislodged before measurements could be taken.

Significantly higher mean airway pressures were recorded when the NHF versus facemask interface was used in both the mouth closed condition (mean 2.7 vs. 0.2 mm H_20; p = 0.001) and the mouth open condition (0.76 vs. 0.39, p =0.001). The closed-mouth airway pressure was significantly greater than the open mouth (2.7 vs. 0.76; p< 0.001) with the NHF interface, but there was no significant difference between the 2 conditions when a facemask was used (0.63 vs. 0.39; p = 0.5).

DISCUSSION:

NHF is a new respiratory support system that has until now been little studied in adults requiring respiratory support. The use of NHF therapy for neonatal care continues to gain increasing acceptance and has shown comparable efficacy to CPAP in this population, while NHF has also demonstrated pressure generating effects in adult volunteers. In this study, significant positive airway pressure was generated by the Optiflow™ NHF system when compared to a traditional facemask at the same flow rates, in adults recovering from surgery. Although the pressure generated was greater when the mouth was closed, it was still significant when the mouth was open.

This trial is the first to demonstrate a positive airway pressure in adults during the use of NHF (previous studies have demonstrated positive airway pressure in healthy adult volunteers), which may have a number of potential clinical benefits as seen with conventional pressure-generating devices. These include improved oxygenation, ventilation-perfusion matching and reduced airway resistance which contribute to decreased work of breathing. Further clinical trials are required to determine the extent to which NHF is associated with such benefits.

CONCLUSION:

NHF generates a significant low-level positive airway pressure in adults, in contrast to a traditional facemask. This may have important clinical implications in improving respiratory support therapy.

KEY POINTS:

- NHF generates a significant positive airway pressure in adult patients who have undergone elective cardiac surgery, while a traditional facemask does not.
- Significant positive airway pressure is generated by NHF when the mouth is open or closed.
- Positive airway pressure generated by NHF may be associated with several clinical benefits including improved oxygenation, ventilation perfusion matching and reduced WOB.

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Parke R, Eccleston M, McGuinness S.
Respir Care. 2011;56(8):1151-1155

The effects of flow on airway pressure during nasal high-flow oxygen therapy.

AIM:

To determine the relationship between air flow from nasal high-flow oxygen therapy (NHF) and mean nasopharyngeal airway pressure in adults.

METHOD:

Adult patients undergoing cardiac surgery were recruited to participate in this prospective, observational, single centre study (n=15). After surgery, patients were fitted with a 10 French catheter into the nasopharynx via the nose while sedated and ventilated in the intensive care unit. The morning after surgery, once the patient was awake, extubated and sitting upright, the catheter was connected to a pressure transducer and NHF was begun using a heated humidified NHF system [Optiflow™; Fisher & Paykel Healthcare]. After an acclimatisation period of 15 min and once breathing had settled, 1 min recordings of nasopharyngeal airway pressure were taken with the patient's mouth both open and closed at flow rates of 30, 40 and 50 L/min. Each patient received NHF at each flow rate according to a standard method of random allocation.

Mean nasopharyngeal airway pressure was the average of pressures from the peak of inspiration of the first breath to the peak of inspiration of the last breath of each 1 min recording.

NHF FLOW RATE (L/MIN)	MEAN (SD) NASOPHARYNGEAL AIRWAY PRESSURE (CM H_2O)		P VALUE
	Mouth closed	Mouth open	
30	1.93 (1.25)	1.03 (0.67)	0.046
40	2.58 (1.54)	1.30 (0.80)	0.03
50	3.31 (1.05)	1.73 (0.82)	<0.001

NHF = nasal high-flow oxygen therapy; SD = standard deviation.

RESULTS:

Twelve patients completed the study. As NHF flow rate increased, airway pressure increased in a positive linear manner, in both the mouth-open and mouth-closed positions. At each flow rate, airway pressure was significantly greater in the mouth-closed position than the mouth-open position (table).

DISCUSSION:

There are currently few data regarding airway pressure generated by NHF and the relationship between flow rate and resultant airway pressure. This study found that mean nasopharyngeal pressure during NHF with Optiflow™ increases as flow rate increases. NHF generates positive airway pressure, and this pressure is greater when the mouth is closed. This latter observation could potentially be explained by higher pressure when the mouth is closed, presumably due to higher resistance to expiration since the expired gas is forced to flow via a restricted path. Higher airway pressure was also observed during inspiration, which could be attributed to pressure in the upper airway being above atmospheric pressure because of the high velocity of incoming gas.

Inter-patient variability in airway pressure was noted in this study, as in previous studies, and this was likely due to variations between patients in nare size relative to nasal interface size. Clinicians prescribing NHF should be aware of this.

Although NHF cannot yet be considered as an alternative to continuous positive airway pressure (CPAP), it could be used as an interim treatment step in selected patients, particularly given its advantages over high-flow face-mask oxygen therapy (HFFM), which include better comfort, improved oxygenation and lower respiratory rates.

CONCLUSION:

In this study of NHF (Optiflow™) for adults after cardiac surgery, there was a positive linear correlation between flow rate and nasopharyngeal airway pressure.

KEY POINTS:

- Airway pressure is significantly positively correlated with the oxygen flow rate when using NHF in adults.
- A positive airway pressure is generated, and airway pressure is higher with the mouth closed than with the mouth open.
- There may be inter-patient variability in airway pressure in patients using NHF.

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Ritchie J, Williams A, Gerard C, Hockey H.
Anaesth Intensive Care. 2011;39(6):1103-1110.

Evaluation of a humidified nasal high flow oxygen system, using oxygraphy, capnography and measurement of upper airway pressures.

AIM:

To define the performance of a humidified nasal high flow oxygen system in healthy volunteers.

METHOD:

A nasal high flow oxygen system (Optiflow™; Fisher & Paykel Healthcare), consisting of a heated humidifier (MR880), heated tubing (RT241) and a nasal interface (RT034), was used for gas delivery. A fixed inspired oxygen fraction (FiO_2) of 0.6 was used throughout the study. A hypopharyngeal catheter was inserted through the nose of each subject under local anaesthesia, from which hypopharyngeal pressures, FiO_2, end-tidal oxygen (FEO_2) and end-tidal carbon dioxide ($FECO_2$) were measured. Recordings were taken after a period of stabilization and then repeated at one minute to ensure a steady state. Measurements were taken for each subject at rest breathing through their nose with the mouth closed, at rest breathing through their mouth, and during a period of exercise on a stationary bicycle where exercise work rate was adjusted to achieve a peak inspiratory flow rate (PIFR) of >100 L/min. Gas flow rates were 10, 20, 30, 40 and 50 L/min, given in a random order.

RESULTS:

Ten healthy adult volunteers were included (8 male and 2 female, aged 23-43 years). There was a significant upward trend for calculated FiO_2 with increasing flow rate for all breathing patterns. For all gas flow rates, calculated FiO_2 was the highest when breathing through the nose at rest and lowest during exercise with a PIFR>90 L/min, with a significant difference between the three breathing patterns ($P<0.001$). $FECO_2$ also varied significantly between the different breathing patterns ($P<0.001$), being highest during exercise and lowest when breathing with the mouth open at rest. Peak pressures were highest when gas flow rate was higher and when breathing with the mouth closed versus open. Looking at individual data, there was an almost linear increase in mean upper airway pressures as gas flow increased above rates of 30 L/min. For flow rates of 30, 40 and 50 L/min, corresponding mean upper airway pressures approached 3, 4 and 5 cmH_2O, respectively.

DISCUSSION:

This study documented the performance of a humidified nasal high flow oxygen system (Optiflow™). The documentation of positive airway pressure provision is a potential mechanism behind the ability of these devices to effectively manage hypoxaemia. The addition of humidity to inspired gases is also another potential mechanism of benefit, but no humidity data were presented in this analysis.

CONCLUSION:

The humidified nasal high flow oxygen system tested delivered prescribed FiO_2 at gas flow rates greater than PIFR. With a closed mouth, the system delivered positive airway pressure which is proportional to the gas flow rate.

KEY POINTS:

- The Optiflow™ humidified nasal high flow oxygen system tested delivers prescribed FiO_2 at gas flow rates greater than PIFR.
- When the mouth is closed, the Optiflow™ humidified nasal high flow oxygen system delivers clinically relevant levels of positive airway pressure proportional to the gas flow rate.

inScience Communications

Mauri T, Turrini C, Eronia N, Grasselli G, Volta CA, Bellani G, Pesenti A
Am J Respir Crit Care Med 2017; 195(9): 1207-1215.

Physiologic effects of nasal high-flow cannula therapy in acute hypoxemic respiratory failure.

AIM:

To compare the effects of nasal high-flow (NHF) cannula treatment with a standard oxygen facial mask on respiratory parameters in acute hypoxemic respiratory failure (AHRF) patients

METHODS:

Patient groups

- Non-intubated AHRF patients with partial pressure of oxygen (PaO_2)/set fraction of inspired oxygen (FiO_2) ≤ 300 mmHg admitted to the intensive care unit (ICU)

Study design

- Prospective randomized cross-over study at a single center

Outcome measures

- Inspiratory effort and work of breathing, ventilation and gas exchange, lung volume, transpulmonary pressures, ventilation homogeneity and air-flows

Treatment regimens

- Patients were entered in a random order into two 20-minute study phases:
  - NHF cannula with heated (37 °C), humidified air/oxygen flow set at 40 L/min
  - Standard non-occlusive oxygen facial mask with air/oxygen flow set at 12 L/min.
- FiO_2 was set to maintain oxygen saturation on pulse oximetry (SpO_2) at 90 to 95% with standard facial mask.
- Set FiO_2 during both study phases was measured using the AIRVO™ 2 system (Fisher & Paykel Healthcare) connected to the NHF cannula or standard facial mask.
- An esophageal balloon catheter was placed in the esophagus of patients to allow for continual recording of esophageal waveforms. Patients were also connected to an electrical impedance tomography (EIT) monitor.
- Patient demographics and baseline clinical data were recorded at enrollment.
- At the end of each study phase, the following parameters were measured: arterial blood gases, hemodynamics, inspiratory effort and work of breathing by esophageal pressure swings (ΔPes) and pressure-time product (PTP) and lung volumes and ventilation homogeneity by EIT.

RESULTS:

Enrolled patients

- Fifteen AHRF patients aged 60 ± 14 years old, 40% (n = 60) female
- All patients had PaO_2/set FiO_2 < 200 mmHg at enrollment, with 3 patients < 100 mmHg.
- Seven patients had bilateral infiltrates on chest X-ray.

Outcomes

NHF cannula treatment significantly reduced inspiratory effort and work of breathing (WOB) (see Table 1).

- ΔPes were significantly lower with NHF cannula compared with the standard facial mask ($p < 0.01$), which indicates a reduction in inspiratory effort.
- PTP and PTPmin were both significantly lower during NHF cannula treatment also ($p < 0.05$ and $p < 0.001$, respectively), which suggests lighter metabolic WOB per breath and per minute
- The V_T/ΔPes ratio (estimate of the dynamic lung compliance) was significantly higher ($p < 0.05$) during NHF cannula treatment, which suggests improved lung mechanics and/or external "ventilation support".

NHF cannula treatment reduced minute ventilation (MV) and improved oxygenation (see Table 1).

- MV and corrected MV (MVcorr = MV* $PaCO_2$/40 mmHg) were significantly lower during NHF cannula treatment compared with the use of a standard facial mask ($p < 0.001$).
- The respiratory rate (RR) was significantly decreased during HFNC ($p < 0.01$), whereas tidal volume (V_T) did not differ between phases.
- NHF cannula treatment significantly increased PaO_2 ($p < 0.001$) with no significant change in $PaCO_2$ and pH.
- A significant correlation existed between reductions in PTP and changes of MVcorr during NHF cannula treatment, which suggests more effective CO_2 clearance and/or reduced CO_2 production.

Mauri T, Turrini C, Eronia N, Grasselli G, Volta CA, Bellani G, Pesenti A
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Table 1: Effects of NHF cannula treatment on work of breathing, ventilation, gas exchange and hemodynamics

VARIABLE	O_2 FACIAL MASK	NHF CANNULA	P-VALUE #
ΔPes (cmH_2O)	9.9 ± 4.2	8.0 ± 3.4	< 0.01
PTP (cmH_2O*s)	9.5 [5.7-12.1]	7.4 [4.1-9.4]	< 0.01
PTPmin (cmH_2O*s/min)	216.3 ± 100.5	154.8 ± 84.8	< 0.001
RR (bpm)	24 [20-27]	22 [17-24]	< 0.01
VT (change from facial mask, %)	-	-5 ± 32	NS
MV (change from facial mask, %)	-	-19 ± 16	< 0.001
MVcorr (change from facial mask, %)	-	-18 ± 15	< 0.001
Set FiO_2	0.60 [0.50-0.75]	0.60 [0.50-0.75]	NS
PaO_2 (mmHg)	72 [68-75]	98 [78-131]	< 0.001
PaO_2/set FiO_2 (mmHg)	130 ± 35	184 ± 53	< 0.001
$PaCO_2$ (mmHg)	40.7 ± 5.7	41.1 ± 5.9	NS
pH	7.45 ± 0.02	7.44 ± 0.03	NS

MV = minute ventilation; $PaCO_2$ = carbon dioxide partial arterial pressure; PaO_2 = oxygen partial arterial pressure;
PaO_2/set FiO_2 = oxygen partial arterial pressure/set oxygen-inspired fraction ratio; ΔPes = inspiratory esophageal pressure swing;
PTP = pressure-time product per breath; PTPmin = pressure-time product per minute; RR = respiratory rate; V_T = tidal volume; NS = non-significant.
Normally distributed variables are expressed as mean ± standard deviation, non-normal ones as median [interquartile range].
P-value by paired t-test or by Wilcoxon's signed rank test, as appropriate.

NHF cannula treatment increased lung volume and transpulmonary pressures, and improved ventilation homogeneity and air-flows (see Table 2).

- Lung volume was significantly increased during NHF cannula treatment ($p \leq 0.01$), which suggests the generation of positive end-expiratory pressure (PEEP).
- End-expiratory transpulmonary pressure (PL,ee) was significantly increased during NHF cannula treatment ($p < 0.001$), which possibly indicates a lower tendency to alveolar collapse.
- A small but significant fall in the global inhomogeneity (GI) ventilation index ($p < 0.01$) was noted during NHF cannula treatment, which indicates improved ventilation homogeneity in the lungs.
- There was a significant reduction in peak expiratory flow (PEF) during NHF cannula treatment ($p \leq 0.001$). Peak inspiratory flow (PIF) was also reduced, though not significantly.
- The ratio of inspiratory time to total time (Ti/Ttot) was significantly lower during NHF cannula treatment ($p < 0.05$), which may suggest a lower tension-time index of the inspiratory muscles.

Mauri T, Turrini C, Eronia N, Grasselli G, Volta CA, Bellani G, Pesenti A
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Table 2: Effects of NHF cannula treatment on lung aeration, homogeneity and respiratory pattern

VARIABLE	O_2 FACIAL MASK	NHF CANNULA	P-VALUE #
$\Delta EELI_{glob}$ (change from facial mask, % of baseline VT)	-	51 ± 57	< 0.001
$\Delta EELI_{non-dep}$ (change from facial mask, % of baseline VT)	-	29 ± 36	≤ 0.001
$\Delta EELI_{dep}$ (change from facial mask, % of baseline VT)	-	26 ± 33	≤ 0.01
$P_{L,ee}$ (cmH_2O)	-10.1 ± 5.0	-7.5 ± 5.2	< 0.001
$P_{L,ei}$ (cmH_2O)	-3.6 ± 4.9	-2.6 ± 4.5	NS
ΔP_L (cmH_2O)	5.7 ± 3.4	4.3 ± 2.9	NS
GI index	0.50 [0.49-0.57]	0.47 [0.43-0.60]	< 0.01
PIF_{glob} (change from facial mask, %)	-	-15 ± 23	NS
PEF_{glob} (change from facial mask, %)		-27 ± 22	≤ 0.001
Ti/Ttot	0.5 ± 0.0	0.4 ± 0.0	< 0.05

$\Delta EELI_{glob}$ = global change of end-expiratory lung impedance; $\Delta EELI_{non-dep}$ = change of end-expiratory lung impedance in non-dependent regions; $\Delta EELI_{dep}$ = change of end-expiratory lung impedance in dependent regions; GI index = global inhomogeneity index; PEF = peak expiratory flow; PIF = peak inspiratory flow; $P_{L,ei}$ = dynamic end-inspiratory transpulmonary pressure; $P_{L,ee}$ =dynamic end-expiratory transpulmonary pressure; ΔPL = driving transpulmonary pressure; Ti = inspiratory time; Ttot = total time; V_T = tidal volume; NS = non-significant.
Normally distributed variables are expressed as mean ± standard deviation, non-normal ones as median [interquartile range].
P-value by paired t-test or by Wilcoxon's signed rank test, as appropriate.

Baseline $PaCO_2$ is correlated with changes in inspiratory effort.

- During NHF cannula treatment, the reduction of inspiratory effort (reflected by ΔPes) was significantly correlated with work of breathing (reflected by PTP) and patients' baseline $PaCO_2$ ($p < 0.01$ and $p < 0.05$, respectively).
- There was no correlation between patients' baseline PaO_2 and either of these variables ($p = 0.42$ and $p = 0.35$).

CONCLUSIONS:

- In AHRF patients, NHF cannula treatment improved gas exchange, lowered respiratory rate and effort, and improved lung volume, dynamic compliance, transpulmonary pressures and homogeneity,
- All of these physiologic benefits might improve the clinical outcomes of AHRF patients

KEY POINTS:

- Inspiratory effort, work of breathing and minute ventilation were significantly reduced by NHF cannula treatment compared with the use of a standard oxygen facial mask in AHRF patients.
- NHF cannula treatment increased lung volume and transpulmonary pressures, and improved oxygenation, ventilation homogeneity and air-flows.
- The physiological effects of NHF cannula treatment in AHRF patients might improve clinical outcomes

Möller W, Feng S, Domanski U, Franke K, Celik G, Bartenstein P, et al.
J Appl Physiol (1985). 2017; 122(1): 191–197.

Nasal high flow reduces dead space.

AIM:

To test the hypothesis that nasal high flow (NHF) therapy in a dose-dependent manner can clear dead space in the upper airways and decrease CO_2 re-breathing

METHODS:

Patient groups

- Two-part study
  - Part 1 — tracer gas scintigraphy study involving healthy, nonsmoking volunteers
  - Part 2 — nasally-breathing tracheotomized patients admitted to hospital for weaning

Study design

- Randomized cross-over study

Outcome measures

- In healthy volunteers, clearance of ^{81m}Kr tracer gas from the upper airways during NHF therapy was assessed using dynamic gamma camera imaging in five regions of interest (ROI): anterior nasal (Nasal1), posterior nasal (Nasal2), pharynx (space from soft palate to the larynx), trachea, and upper lung
  - Nasal clearance rates were derived from time constants and MRI-measured nasal volumes (VN)
- In tracheotomized patients, reduction of re-breathing during NHF therapy was investigated using volumetric capnography and oximetry by sampling gas from the trachea region
  - The effect of NHF therapy on the volume of inspired O_2 and CO_2 was analyzed for every breath
  - Arterial blood oxygen saturation (SpO_2) and transcutaneous CO_2 were also monitored

Treatment regimens

- NHF therapy was delivered using the AIRVO™ blower-humidifier and the Optiflow™ nasal cannula (Fisher & Paykel Healthcare) at rates of 15, 30, and 45 L/min in a randomized order
  - In the scintigraphy study, NHF was delivered for 30 seconds (during breath holding with closed mouth)
  - In tracheotomized patients, NHF was delivered continuously for 10 minutes, also with closed mouth

RESULTS:

Enrolled patients

- Part 1 — 10 healthy, nonsmoking volunteers, mean age (± SD) 55 ± 14 years
- Part 2 — 3 nasally-breathing tracheotomized male patients not requiring supplemental O_2, admitted to hospital for weaning
  - Two patients (aged 59 and 72 years) had chronic obstructive pulmonary disease (COPD); the third patient (72 years) was recovering from subarachnoid hemorrhage and pneumonia

Outcomes

^{81m}Kr gas clearance in healthy volunteers

- An increase in NHF therapy flow rate from 15 to 45 L/min was associated with an increase in clearance of the ^{81m}Kr gas from the nasal cavities of all participants [Pearson's correlation coefficient (cc) = -0.55, $P < 0.01$] (see Table 1)
  - Nasal1 region cleared significantly faster than Nasal2 ($P < 0.01$); however, there was no apparent correlation between clearance half-times and individual nasal volumes (VN)
- Nasal clearance rates were calculated using the time constants for both ROIs and VN: 40.6 ± 12.3, 52.5 ± 17.7, and 72.9 ± 21.3 ml/s during NHF rates of 15, 30, and 45 L/min, respectively
  - A significant correlation was demonstrated between clearance rate and NHF therapy (cc = 0.61, $P < 0.01$)
- NHF therapy-induced ^{81m}Kr gas clearance was slower in the lower compartments beyond the soft palate (pharynx, cc = 0.41, $P < 0.01$; trachea, cc = -0.51, $P < 0.01$)
  - Pharyngeal and tracheal clearance rates correlated with the nasal clearance rates (cc = 0.4, $P < 0.05$)
  - No ^{81m}Kr gas clearance was observed in the upper lung

Table 1: ^{81m}Kr gas clearance in the anterior and posterior regions of the nasal cavity, pharynx, and trachea regions of interest (ROI) of healthy volunteers during NHF therapy flow rates of 15, 30, and 45 L/min

HALF-TIME $T_{1/2}$, S			
ROI	**NHF 15 L/min**	**NHF 30 L/min**	**NHF 45 L/min**
Nasal1	0.70 ± 0.26	0.53 ± 0.17	0.39 ± 0.11
Nasal2	0.91 ± 0.34*	0.69 ± 0.24*	0.48 ± 0.11*
Pharynx	7.80 ± 2.96	6.19 ± 3.82	4.43 ± 2.92
Trachea	23.73 ± 6.63	14.30 ± 13.43	10.53 ± 9.85

Values are means ± SD. In all compartments, half-times correlated with NHF (Nasal1, cc = -0.55, P < 0.01; Nasal2, cc = -0.57, P < 0.01; pharynx, cc = -0.41, P < 0.01; trachea, cc = -0.51, P < 0.01). Nasal1 and Nasal2, anterior and posterior parts of nasal cavity, respectively. * P < 0.05 Nasal2 vs. Nasal1, paired t-test.

Re-breathing of expired air during NHF therapy in tracheotomized patients

- In all three patients, NHF therapy resulted in a decrease of inspired CO_2 and an increase of inspired O_2 in a flow-dependent manner
  - NHF-induced decrease of inspired CO_2 correlated with an increase of inspired O_2 (cc = -0.77, P = 0.016)
- The ratio between inspired CO_2 in the first 100 ml of inspired volume and the total inspired CO_2 was significantly higher during NHF therapy relative to baseline ventilation (0.84 ± 0.10 vs. 0.75 ± 0.12; P < 0.01, paired t-test)
- Table 2 shows the change of tidal volume, respiratory rate, minute ventilation, SpO_2, and tissue CO_2 throughout the study

Möller W, Feng S, Domanski U, Franke K, Celik G, Bartenstein P, et al.
J Appl Physiol (1985). 2017; 122(1): 191–197.

Table 2: Change of ventilation parameters, peripheral capillary O_2 saturation, and tissue CO_2 in three patients receiving NHF therapy at flow rates of 15, 30, and 45 L/min

	15 L/min		30 L/min		45 L/min	
	BASELINE	NHF	BASELINE	NHF	BASELINE	NHF
PATIENT A						
Tidal volume, ml	332.0	282.6	348.7	300.4	331.5	191.7
Respiratory rate, min^{-1}	10.9	12.2	12.3	10.6	12.3	10.8
Minute ventilation, L/min	3.6	3.4	4.3	3.2	4.1	2.1
SpO_2, %	96.1	96.4	96.8	96.6	96.9	97.1
Tissue CO_2, mmHg	32.0	31.8	31.3	31.2	30.7	30.6
PATIENT B						
Tidal volume, ml	366.7	289.7	438.5	364.3	334.6	332.3
Respiratory rate, min^{-1}	12.9	14.3	12.2	12.4	15.0	14.8
Minute ventilation, L/min	4.7	4.1	5.4	4.5	5.0	4.9
SpO_2, %	92.6	92.2	92.9	92.8	93.5	94.6
Tissue CO_2, mmHg	48.2	49.1	48.0	48.7	48.7	48.3
PATIENT C						
Tidal volume, ml	290.1	264.1	333.0	255.6	391.1	247.6
Respiratory rate, min^{-1}	14.1	13.2	12.2	12.1	14.0	12.3
Minute ventilation, L/min	4.1	3.5	4.1	3.1	5.5	3.0
SpO_2, %	96.6	96.5	97.4	97.6	97.0	97.0
Tissue CO_2, mmHg	39.2	38.5	41.2	40.0	38.3	37.8

CONCLUSIONS:

- NHF therapy reduces dead space by clearing expired air from the upper airways. This leads to reduced re-breathing and improvements in alveolar ventilation and gas exchange
- It is anticipated that an improved gas exchange results in a reduced minute ventilation and/or the normalizing of arterial blood gas (ABG)
- Clearance of the dead space is flow- and time-dependent and may extend below the soft palate

KEY POINTS:

- An increase in the NHF therapy flow rate from 15 to 45 L/min was associated with an increase in clearance of the ^{81m}Kr gas from the nasal cavity
- A significant correlation was demonstrated between nasal clearance and NHF therapy rates and durations
- Gas clearance was slower but still NHF-dependent in the lower compartments beyond the soft palate

Pisani L, Fasano L, Corcione N, Comellini V, Musti M, Brandao M, et al.
Thorax. 2017 Apr;72(4):373-375.

Change in pulmonary mechanics and the effect on breathing pattern of high flow oxygen therapy in stable hypercapnic COPD.

AIM:

To compare the physiological effects of standard oxygen therapy, noninvasive ventilation (NIV) and nasal high flow (NHF) therapy in patients with stable chronic hypercapnic respiratory failure (CHRF) and COPD

METHOD:

Patient group

- COPD outpatients with stable CHRF

Study design

- Prospective randomized study at a single center

Outcome measures

- Breathing pattern, arterial blood gases (ABGs), and inspiratory effort, determined from transdiaphragmatic pressure (Pdi) tracing
  - Measures were taken at baseline and during five study periods (each 30 minutes in duration)

Treatment regimen

- NIV administered through a full-face mask. Expiratory pressure (EPAP) set at 4 cmH_2O and peak inspiratory pressure (IPAP) set according to tolerance and to avoid tidal volumes > 7 ml/kg
- NHF therapy [AIRVO™ system with Optiflow™ nasal interface (Fisher & Paykel Healthcare)] at two flow rates, 20 and 30 L/min at 37 °C
  - At each flow rate, patients were asked to breathe with their mouth open or closed
- Each patient underwent the five 30-minute study periods — according to a random sequence
  - During the trials, oxygen was administered to maintain oxygen saturation (SpO_2) between 91% and 94%, keeping the fraction of inspired oxygen (FiO_2) constant
  - After each trial, standard oxygen therapy was administered through a nasal cannula for 10 minutes (baseline)

RESULTS:

Enrolled patients

- Fourteen consecutive COPD patients with stable CHRF, mean age (± SD) 73.5 ± 5.2 years (9 males), were enrolled in the study

Outcomes

- Compared with baseline (standard oxygen), a significant reduction in breathing frequency was observed with both NHF therapy (closed mouth) and NIV (see table)
- For all settings, each patient's own expiratory time (TE,p) was significantly prolonged and tidal volumes (V_T) were higher compared with baseline
  - No difference in the patient's own inspiratory time (TI,p) was observed between study periods
- Compared with baseline, there was a reduction in both Pdi swing and diaphragm pressure time product (PTPdi) in all study periods
  - Significantly greater reductions were observed during NIV, compared with NHF therapy
- A significant reduction in dynamic intrinsic positive end expiratory pressure (PEEPi, dyn) was observed in all trials compared with baseline
- There was no change in breathing frequency, TI,p and TE,p, between the NHF therapy study periods with the mouth closed or open
  - Pdi at an NHF rate of 20 L/min was statistically higher with the closed mouth compared with open
- A non-significant decrease in partial pressure of carbon dioxide ($PaCO_2$) level was observed with NHF therapy at 30 L/min and NIV compared with standard oxygen
- There was no difference in patient comfort between NHF therapy and NIV

Pisani L, Fasano L, Corcione N, Comellini V, Musti M, Brandao M, et al.
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VARIABLE	BASELINE	NHF 20 (closed)	NHF 20 (open)	NHF 30 (closed)	NHF 30 (open)	NIV
TI,p (seconds)	0.95 ± 0.2	0.85 ± 0.4	0.96 ± 0.2	0.94 ± 0.3	0.92 ± 0.3	1.00 ± 0.2
TE,p (seconds)	1.94 ± 0.4	2.35 ± 0.4*	2.19 ± 0.5*	2.30 ± 0.5*	2.20 ± 0.3*	2.61 ± 1.0*
Breathing frequency (breaths/min)	24.8 ± 2.3	19.01 ± 5.2†	20.8 ± 5.8	18.7 ± 3.6†	19.64 ± 2.8	17.8 ± 3.8†
Tidal volume (mL)	314.50 ± 84	391.22 ± 106‡		364.22 ± 66.0		456.20 ± 100‡
Pdi swing (cmH_2O)	13.5 ± 6.7	8.7 ± 4.1§	12.0 ± 5.8	8.2 ± 3.7§	10.2 ± 5.2§	5.1 ± 2.2§¶
PTPdi/min (cmH_2Oxs/min)	238.3 ± 82.1	164.2 ± 51.3**	172.7 ± 45.4**	143.2 ± 48.9**	157.3 ± 56.9**	101.7 ± 42.9**††
PEEPi,dyn (cmH_2O)	2.12 ± 0.9	1.48 ± 0.7‡‡		1.03 ± 0.6‡‡		0.9 ± 0.002††

* P = 0.006 NHF 20 closed vs. baseline; P = 0.01 NHF 20 open vs. baseline; P = 0.007 NHF 30 closed vs. baseline; P = 0.02 NHF 30 open vs. baseline; P = 0.002 NIV vs. baseline. † P = 0.022 NHF 20 closed vs. baseline; P = 0.007 NHF 30 closed vs. baseline; P = 0.002 NIV vs. baseline. ‡ P = 0.015 NHF 20 closed vs. baseline; P = 0.007 NIV vs. baseline. § P = 0.005 NHF 20 closed vs. baseline; P = 0.005 NHF 30 closed vs. baseline; P = 0.03 NHF 30 open vs. baseline; P = 0.001 NIV vs. baseline. ¶ P < 0.003 NIV vs. NHF 20 closed; P = 0.003 NIV vs. NHF 20 open; P= 0.007 NIV vs. NHF 30 closed; P = 0.005 NIV vs. NHF 30 open. ** P = 0.005 NHF 20 closed vs. baseline; P = 0.002 NHF 20 open vs. baseline; P = 0.004 NHF 30 closed vs. baseline; P = 0.015 HFOT 30 open vs. baseline; P = 0.001 NIV vs. baseline. †† P < 0.004 NIV vs. HFOT 20 closed; P = 0.006 NIV vs. NHF 20 open; P = 0.016 NIV vs. NHF 30 closed; P = 0.02 NIV vs. NHF 30 open. ‡‡ P = 0.01 NHF 20 closed vs. baseline; P = 0.003 NHF 30 closed vs. baseline; P = 0.001 NIV vs. baseline.
Data is presented as mean ± SD.
NHF, nasal high flow therapy; NIV, noninvasive ventilation; Pdi, transdiaphragmatic pressure; PEEPi,dyn, intrinsic dynamic positive end expiratory pressure; PTPdi, pressure–time product of the transdiaphragmatic; TE,p, patient's expiratory time; TI,p, patient's inspiratory time.

CONCLUSIONS:

- Similar acute physiological changes were observed between NHF therapy and NIV
- Further studies are required to assess the effectiveness of NHF therapy versus NIV in COPD patients with stable hypercapnia

KEY POINTS:

- Compared with standard oxygen, both NHF therapy and NIV significantly improved the breathing pattern and reduced inspiratory effort
- A decrease in $PaCO_2$ was observed with NHF therapy and NIV compared with standard oxygen; however, this was not significant
- There was no apparent difference in patient comfort between NHF therapy and NIV

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