



Adult Nasal High Flow: Clinical paper summaries



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Adult Nasal High Flow PubMed links

SPECIFIC PATIENT POPULATION

- PubMed** 1. [Corley A](#), Caruana L, Barnett A, Tronstad O, Fraser J. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. *Br J Anaesth*. 2011;107(6):998-1004.
- PubMed** 2. [Lenglet H](#), Sztrymf B, Leroy C, Brun P, Dreyfuss D, Ricard J. Humidified high flow nasal oxygen during respiratory failure in the emergency department: feasibility and efficacy. *Respir Care*. 2012;57(11):1873-1878.
- PubMed** 3. [Lucangelo U](#), Vassallo F, Marras E, Ferluga M, Beziza E, Comuzzi L, et al. High-flow nasal interface improves oxygenation in patients undergoing bronchoscopy. *Crit Care Res Pract*. 2012;2012:1-6.
- PubMed** 4. [Parke R](#), McGuinness S, Eccleston M. Nasal high-flow therapy delivers low level positive airway pressure. *British Journal of Anaesthesia*. 2009;103(6):886-890.
- PubMed** 5. [Peters S](#), Holets S, Gay P. Nasal high flow oxygen therapy in do-not-intubate patients with hypoxemic respiratory distress. *Respir Care*. 2013 ; 58(4): 597-600.
- PubMed** 6. [Rea H](#), McAuley S, Jayaram L. The clinical utility of long-term humidification therapy in chronic airway disease. *Respir Med*. 2010;104(4):525-533.
- PubMed** 7. [Roca O](#), Riera J, Torres F et al. High-flow oxygen therapy in acute respiratory failure. *Respir Care*. 2010;55(4):408-13.
- PubMed** 8. [Roca O](#), Pérez-Terán P, Masclans J, Pérez L, Galve E, Evangelista A et al. Patients with New York Heart Association class III heart failure may benefit with high flow nasal cannula supportive therapy. *J Crit Care*. 2013;28(5):741-746.
- PubMed** 9. [Sztrymf B](#), Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D et al. Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. *Intensive Care Med*. 2011;37(11):1780-1786.
- PubMed** 10. [Maggiore S](#), Idone F, Vaschetto R, Festa R, Cataldo A, Antonicelli F et al. Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation. Effects on Oxygenation, Comfort, and Clinical Outcome. *Am J Respir Crit Care Med*. 2014;190(3):282-288.
- PubMed** 11. [Frat J](#), Thille A, Mercat A, Girault C, Ragot S, Perbet S et al. High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure. *N Engl J Med*. 2015;372(23):2185-2196.
- PubMed** 12. [Stéphan F](#), Barrucand B, Petit P, Rézaiguia-Delclaux S, Médard A, Delannoy B et al. High-Flow Nasal Oxygen vs Noninvasive Positive Airway Pressure in Hypoxemic Patients After Cardiothoracic Surgery. *JAMA*. 2015;313(23):2331.

- PubMed** 13. [Hernández G](#), Vaquero C, González P, Subira C, Frutos-Vivar F, Rialp G et al. Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients. *JAMA*. 2016;315(13):1354.
- PubMed** 14. [Hernández G](#), Vaquero C, Colinas L, Cuenca R, González P, Canabal A et al. Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients. *JAMA*. 2016;316(15):1565.

MECHANISMS OF ACTION

- PubMed** 15. [Bräunlich J](#), Köhler M, Wirtz H. Nasal highflow improves ventilation in patients with COPD. *International Journal of Chronic Obstructive Pulmonary Disease*. 2016;:1077.
- PubMed** 16. [Hasani A](#), Chapman T, McCool D, Smith R, Dilworth J, Agnew J. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. *Chron Respir Dis*. 2008;5(2):81-86.
- PubMed** 17. [Mündel T](#), Feng S, Tatkov S, Schneider H. Mechanisms of nasal high flow on ventilation during wakefulness and sleep. *J Appl Physiol*. 2013;114(8):1058-1065.
- PubMed** 18. [Parke R](#), McGuinness S, Eccleston M. A Preliminary Randomized Controlled Trial to Assess Effectiveness of Nasal High-Flow Oxygen in Intensive Care Patients. *Respir Care*. 2011;56(3):265-270.
- PubMed** 19. [Parke R](#), Eccleston M, McGuinness S. The Effects of Flow on Airway Pressure During Nasal High-Flow Oxygen Therapy. *Respir Care*. 2011;56(8):1151-1155.
- PubMed** 20. [Ritchie J](#), Williams A, Gerard C, Hockey H. Evaluation of a humidified nasal high-flow oxygen system, using oxygraphy, capnography and measurement of upper airway pressures. *Anaesth Intensive Care*. 2011;39(6):1103-10



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 (P_{aw}) 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. P_{aw} 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 and 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 $\geq 95\%$, 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 P_{aw} , 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 P_{aw} 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/m² versus 24.4% in those with BMI of 40 kg/m²].

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
P_{aw} (cm H ₂ O)	-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; P_{aw} = airway pressure; SD = standard deviation.

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-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-oxygen therapy.
- Benefits of HFOT were greatest in patients with a higher BMI.



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 (FiO₂) 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 O₂ 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 FiO₂ ≥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 SpO₂ 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 SpO₂ (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 PaO₂ (p<0.05), but no change in PCO₂ 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.



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.

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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) $\geq 90\%$ 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). Fiberoptic 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 detected with N60.

S3. Lucangelo U, Vassallo F, Marras E, Ferluga M, Beziza E, Comuzzi L et al. High-Flow Nasal Interface Improves Oxygenation in Patients Undergoing Bronchoscopy. Crit Care Res Pract. 2012;2012:1-6.



MEDIAN (1ST-3RD QUARTILE)	BASELINE	END OF BRONCHOSCOPY	10 MINUTES AFTER BRONCHOSCOPY
PaCO₂ (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)
PaO₂/FiO₂			
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 PO₂			
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
PaO₂ (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}
SpO₂ (%)			
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 PO₂, ratio between arterial and alveolar oxygen pressure; HR, heart rate; MAP, mean arterial pressure; PaCO₂, arterial pressure of carbon dioxide; PaO₂/FiO₂, ratio between arterial oxygen pressure and inspiratory fraction of oxygen; SpO₂, 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.

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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 (FiO₂) were titrated to achieve an oxygen saturation by pulse oximetry (SpO₂) or arterial blood gas (SaO₂) of ≥95%. Patients in the HFFM group received oxygen at 31°C and 32 mg H₂O/L also titrated to achieve SpO₂ or SaO₂ of ≥95%. Variables assessed were rate of transfer to noninvasive ventilation (NIV), the partial pressure of arterial oxygen (PaO₂)/FiO₂ ratio, SpO₂ 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 PaO₂/FiO₂, time to ICU discharge or hospital stay.

	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.



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.

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.



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, $\text{pH} > 7.28$) 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 HFNC 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; PaCO₂, arterial pressure of carbon dioxide; PaO₂, 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.

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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.



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 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.



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 [SpO₂] <96% while receiving humidified oxygen via FM with a fraction of inspired oxygen [FiO₂] 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 FiO₂ 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 SpO₂ 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 (PaO₂) 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.



	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; FiO₂ = fraction of inspired oxygen; HCO₃⁻ = blood bicarbonate; IQR = interquartile range; PaO₂ = partial pressure of oxygen; PaCO₂ = partial pressure of carbon dioxide; SpO₂ = blood oxygen saturation as measured via pulse oximetry.



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.

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.



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 $\leq 45\%$. 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*

* $p = 0.02$



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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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 (FiO₂) 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

FiO₂ = fraction of inspired oxygen; PaO₂ = partial pressure of oxygen; PaCO₂ = partial pressure of carbon dioxide; SD = standard deviation.

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 SpO₂, PaO₂ and PaO₂/FiO₂ 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.

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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 $\text{PaO}_2/\text{FiO}_2\text{SET}$ 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, $\text{PaO}_2/\text{FiO}_2\text{SET}$ 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 ($p \leq 0.01$); 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).



VARIABLE	OXYGEN THERAPY		P-VALUE
	Venturi mask (n=52)	NHF (n=53)	
OXYGENATION			
PaO₂/FiO₂SET, 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 ₂ SET, % ^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; FiO₂SET, set inspired oxygen fraction; ICU, intensive care unit; PaO₂, arterial oxygen tension; patient.



CONCLUSION:

The results of this study show that use of NHF after extubation results in an improved PaO₂/FiO₂SET ratio for the same set FiO₂ 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 % FiO₂ 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.

KEY POINTS

- Use of NHF post extubation results in better oxygenation for the same set FiO₂ 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.

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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 $\geq 92\%$. 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 $\text{PaO}_2:\text{FiO}_2 \leq 200$ 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.



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. FiO₂, fraction of inspired oxygen; ICU, intensive care unit; NHF, nasal high flow; NIV, noninvasive ventilation; PaO₂, 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 PaO₂:FiO₂ ≤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 PaO₂:FiO₂ 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.



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 (SaO₂) for both arms was set at 92%–98%. The initial NHF flow rate was 50 L/min with an initial fraction of inspired oxygen (FiO₂) of 50%, which was then adjusted to maintain the target saturations. BPAP was initiated at 8 cmH₂O 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 cmH₂O and FiO₂ of 0.5, and then adjusted to maintain the target SaO₂. 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 SaO₂. Allocated treatment could be discontinued when SaO₂ was ≥95% at 6 L/min, PaO₂:FiO₂ 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 (PaCO₂), pH, dyspnea score, comfort score, the number of nurse interventions per patient, ICU stay, or the rate of complications.



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)]			
PaO₂:FiO₂			
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	
FiO₂			
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	

^ap=0.003; ^bp=0.50; ^cp=0.99; ^dp=0.15; ^ep=0.04; ^fp=0.66; ^gp<0.001 vs baseline; ^hp=0.004 vs baseline; ⁱp<0.01; ^jp<0.001 vs 1 hour; ^kp<0.001; ^lp=0.16
BPAP, bilevel positive airway pressure; CI, confidence interval; FiO₂, fraction of inspired oxygen; ICU, intensive care unit; NHF, nasal high flow; PaO₂, 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.

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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 (FiO₂) was adjusted to maintain peripheral oxygen saturation (SpO₂) 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.



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/m²; 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 (FiO₂) was adjusted to achieve a peripheral capillary oxygen saturation (SpO₂) >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, Resironics 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 [SaO₂] 92% and pH 7.35), and FiO₂ adjusted to maintain SpO₂ >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.

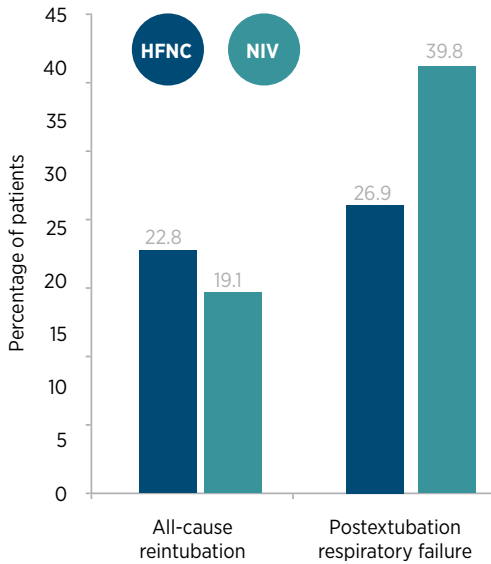


Figure 1. Primary outcomes within 72 hours of extubation among critically ill patients at high risk of extubation failure who received HFNC or NIV therapy. HFNC, high-flow nasal cannula; NIV, noninvasive ventilation.

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].

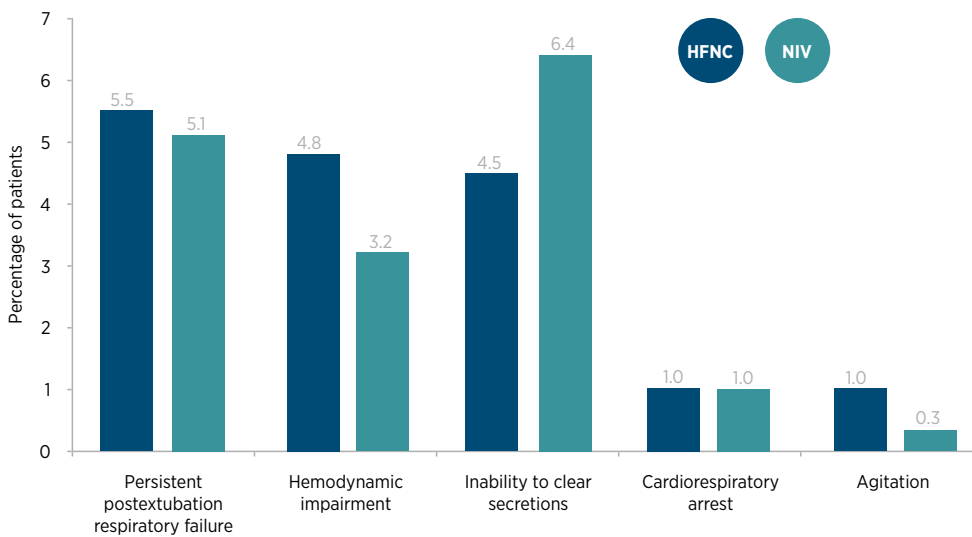


Figure 2 (A). Causes for reintubation within 72 hours of extubation among patients at high risk of extubation failure. HFNC, high-flow nasal cannula; NIV, noninvasive ventilation. *Glasgow Coma Scale score decrease >1 point.

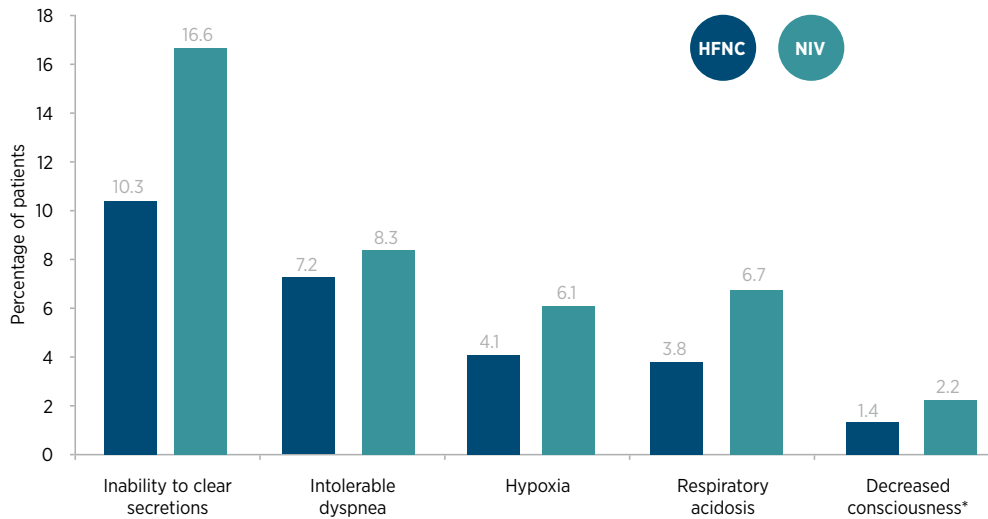


Figure 2 (B). Postextubation respiratory failure within 72 hours of extubation among patients at high risk of extubation failure. HFNC, high-flow nasal cannula; NIV, noninvasive ventilation. *Glasgow Coma Scale score decrease >1 point.

Adverse events leading to treatment discontinuation for ≥ 18 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).

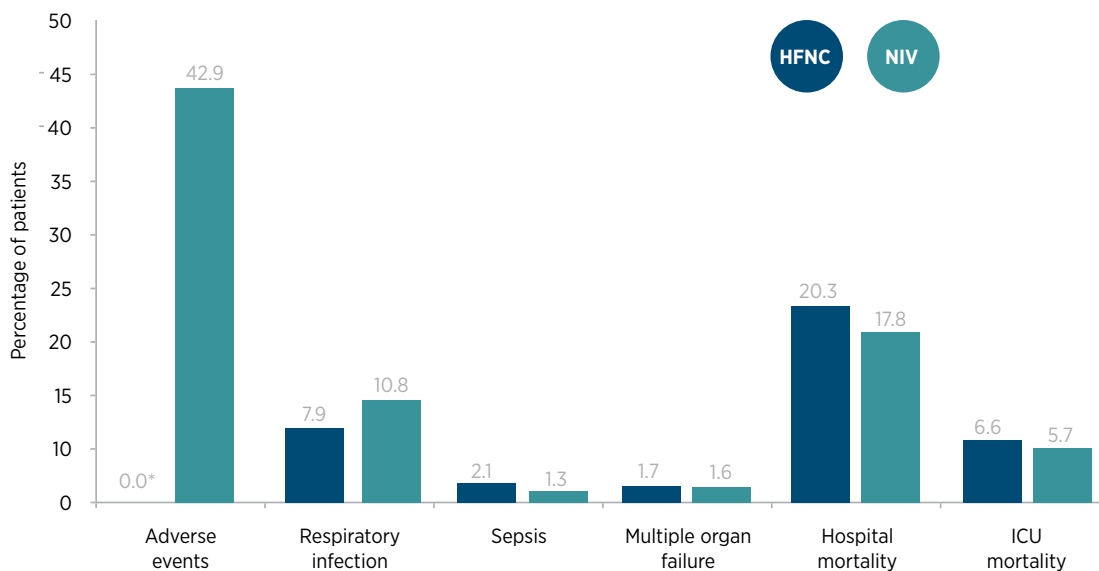


Figure 3. Incidence of adverse events requiring discontinuation for ≥ 18 hours and other secondary outcomes among patients at high risk of extubation failure. HFNC, high-flow nasal cannula; ICU, intensive care unit; NIV, noninvasive ventilation. * $p<0.001$.



Nasal highflow 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 (Respirace; 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).

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 pCO₂ 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 pCO₂ 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 pO₂ 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.

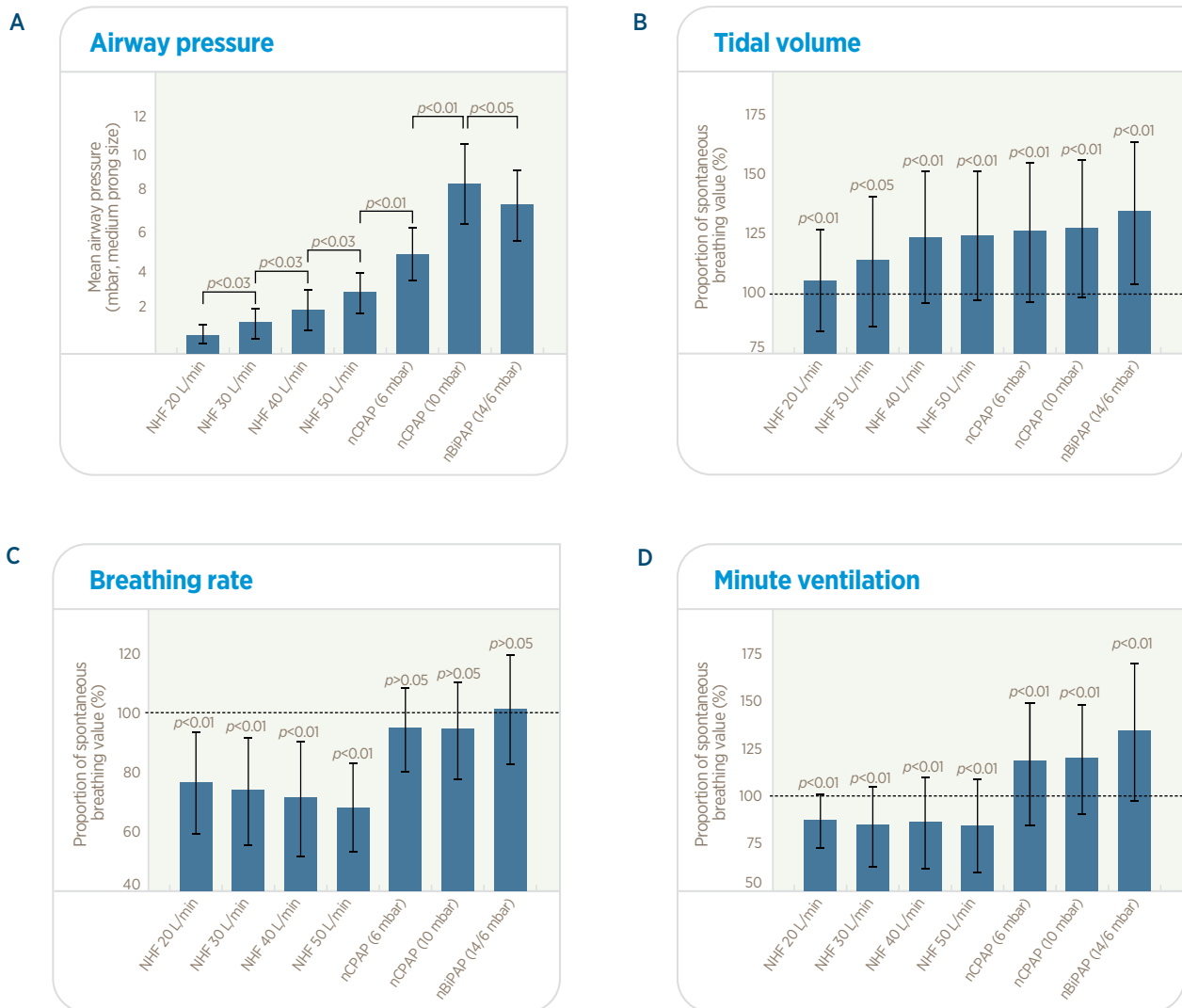


Figure 1. A, mean airway pressure (p-value refers to comparison with previous applied device); B-D, proportion of spontaneous breathing value (p-values in comparison with spontaneous breathing) for B, tidal volume; C, breathing rate; D, minute ventilation. NHF, nasal high flow using medium prongs; nBiPAP,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

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 than for nCPAP and nBiPAP, 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 $p\text{CO}_2$, with fresh air, low in $p\text{CO}_2$, 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 pCO₂ 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 pCO₂, thereby enhancing effectiveness of breathing in patients with COPD and hypercapnia.
- NHF ventilation support leads to a flow-dependent reduction in pCO₂ in patients with COPD and hypercapnia.
- Higher air flow is likely to cause a washout of the respiratory tract, replacing high-pCO₂ exhaled air with low-pCO₂ fresh air, thereby reducing hypercapnia.
- Overall, patients felt NHF was more comfortable and better at reducing dyspnea than nCPAP or nBiPAP.



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.



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.

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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 H₂O) 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® O₂ 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 H₂O; $p = 0.001$) 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.



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.

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).

NHF FLOW RATE (L/MIN)	MEAN (SD) NASOPHARYNGEAL AIRWAY PRESSURE (CM H ₂ O)		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.

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.



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 (FiO₂) 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, FiO₂, end-tidal oxygen (FEO₂) and end-tidal carbon dioxide (FECO₂) 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 FiO₂ with increasing flow rate for all breathing patterns. For all gas flow rates, calculated FiO₂ 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). FECO₂ 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 cmH₂O, 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 FiO₂ 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 FiO₂ 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.

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Definitions

Absolute humidity	The amount of water vapour in a given volume of gas
Acute respiratory distress syndrome (ARDS)	An acute, diffuse, inflammatory lung injury, leading to increased pulmonary vascular permeability, increased lung weight and loss of aerated tissue. The clinical hallmarks are hypoxemia, radiographic opacity in both lungs, increased dead space and reduced compliance in the lung
Acute respiratory failure (ARF)	A syndrome in which the respiratory system fails in one or both of its gas exchange functions: oxygenation and carbon dioxide elimination. Acute respiratory failure is characterised by life threatening derangements in arterial blood gases and acid-base status
Airway pressure (Paw)	Pressure in the airway
Arterial/alveolar oxygen pressure (a/A PO₂)	Ratio between arterial and alveolar oxygen pressure
Arterial carbon dioxide tension (PaCO₂)	The part of total blood gas pressure exerted by carbon dioxide gas; a measure of how much carbon dioxide is dissolved in the blood and how well carbon dioxide is able to move out of the body
Arterial oxygen tension (PaO₂)	The part of total blood gas pressure exerted by oxygen gas; a measure of how much oxygen is dissolved in the blood and how well oxygen is able to move from the airspace of the lungs into the blood
Bilevel positive airway pressure (BPAP)	Positive airway pressure therapy where two pressure levels are applied, one for inspiration and a lower pressure for expiration
Bronchiectasis	A chronic inflammatory condition or degenerative disease of the bronchi which causes localized, irreversible dilation of part of the bronchial tree, resulting in airflow obstruction and impaired mucous clearance
Chronic obstructive pulmonary disease (COPD)	A progressive disease in which the small airways become narrowed, limiting airflow to and from the lungs and causing shortness of breath. In contrast to asthma, air flow limitation in COPD is poorly reversible
Computed tomography	Three-dimensional medical imaging
Confidence interval (CI) 95%	A statistical measure showing that 95% of the results for that parameter lie within the range quoted
Continuous positive airway pressure (CPAP)	A technique of respiratory therapy in which airway pressure is maintained above atmospheric pressure throughout the respiratory cycle by pressurization of the ventilatory circuit
Deadspace	The space in the trachea, bronchi, and other air passages which contains air that does not reach the alveoli during respiration
Dyspnea	Labored breathing or shortness of breath



Electrical impedance tomography (EIT)	A non-invasive, real-time imaging method that produces cross-sectional images of the lung during ventilation
End-expiratory lung impedance (EELI)	Impedance during EIT at the end-expiratory position; used as indirect measure of end-expiratory lung volume
End-expiratory lung volume (EELV)	The volume in the lungs at the end-expiratory position
End-tidal carbon dioxide (FECO₂)	Pressure of carbon dioxide at the end of exhalation
End-tidal oxygen (FEO₂)	Pressure of oxygen at the end of exhalation
Forced expiratory volume in 1 second (FEV1)	The volume of air that can be exhaled during the first second of a forced exhalation
Forced vital capacity (FVC)	The determination of the vital capacity from a maximally forced expiratory effort
Fractional inspired carbon dioxide concentration (FiCO₂)	The fraction of carbon dioxide in inspired gas
Fraction of inspired oxygen (FiO₂)	The proportion of oxygen in the air that is inspired
Heated humidifier (HH)	A device that actively adds heat and water vapor to inspired gas
High-flow face mask (HFFM)	A full-face mask that is used to deliver high-flow gases to a patient during ventilatory support
High-flow nasal cannula (HFNC)	Nasal cannula (a small, half-moon shaped plastic tube, the ends of which fit into the nostrils of a patient) designed to deliver gas at a high range of flows
High-flow nasal cannula oxygen therapy (HFNC)	A technique to provide a range of flows of heated, humidified oxygen and air to patients requiring respiratory support, delivered through nasal cannulae
High-flow oxygen therapy (HFOT)	Delivery of oxygen gas at a high flow rate
Hypercapnia	The presence of an abnormally high level of carbon dioxide in the circulating blood
Idiopathic pulmonary fibrosis (IPF)	A disease where the air sacs of the lungs (alveoli) and lung tissue become damaged and scarred, which results in shortness of breath
Intensive care unit (ICU)	A hospital facility providing intensive nursing and medical care for critically ill patients
Intention to treat analysis (ITT)	Non inferiority study
Interquartile range (IQR)	A descriptive statistic to measure statistical dispersion, being equal to the difference between the third and first quartiles
Mechanical ventilation (MV)	The use of an invasive artificial airway to mechanically assist or replace spontaneous breathing, when patients cannot do so on their own
Minute volume (also known as minute ventilation)	The volume of gas that moves in and out of the lungs in one minute; it is calculated by multiplying the exhaled tidal volume by the respiratory rate
Nasal high flow oxygen therapy (NHF)	A technique to provide a high flow of heated, humidified oxygen and air to patients requiring respiratory support, delivered through nasal cannulae



Nasal oxygen cannula	A small, half-moon shaped plastic tube, the ends of which fit into the nostrils of a patient, which is used to deliver oxygen at a concentration higher than that in ambient air
Noninvasive ventilation (NIV)	The delivery of ventilatory support without the need for an invasive artificial airway
Oxygen saturation (SpO₂)	The amount of oxygen attached to the haemoglobin cell in the circulatory system (as a %)
Oxygen saturation (SaO₂)	Oxygen saturation of the hemoglobin of arterial blood
Oxygen saturation by pulse oximetry (SpO₂)	Oxygen saturation as measured by pulse oximetry (as a %)
Partial pressure of arterial carbon dioxide (PaCO₂)	The part of total blood gas pressure exerted by carbon dioxide gas; a measure of how much carbon dioxide is dissolved in the blood and how well carbon dioxide is able to move from the airspace of the lungs into the blood
Partial pressure of arterial oxygen (PaO₂)	The part of total blood gas pressure exerted by oxygen gas; a measure of how much oxygen is dissolved in the blood and how well oxygen is able to move from the airspace of the lungs into the blood
Peak inspiratory flow rate (PIFR)	Maximum flow rate achieved during inspiration
pH	A measure of acidity or alkalinity
Pneumothorax	Air or gas in the pleural space
Positive end-expiratory pressure (PEEP)	The amount of pressure above atmospheric pressure present in the airway at the end of the expiratory cycle during mechanical ventilation
Radio-aerosol movement	Reflects the rate of clearance of inhaled radio-aerosol particles from the lung
Relative humidity (RH)	The maximum amount of water a gas can hold at a given temperature
Tidal volume (VT)	The volume inspired or expired per breath
Tidal impedance variation (VART)	The difference between impedance at the end of inspiration and expiration
Tracheobronchial clearance	Particle clearance from the ciliated conducting airways (tracheobronchial region)
Visual analogue scale (VAS)	A technique to assess subjective levels of pain or discomfort on an increasing scale, with visual cues for the patient that are related to a numerical value.
Work of breathing (WOB)	The force required to expand the lung against its elastic properties

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