

**Nasal High Flow:
Evidence & Application**

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Disclosures

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Crazy about the New Zealand All Blacks Rugby Team

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Outline

- 1 What are the origins of HFNC?

- 2 What are the mechanisms of action?

- 3 How can high flow be used effectively in your ED? ▲ COVID-19

- 4 Q & A

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*Q1: Who routinely used HFNC in their ED
before COVID-19?*

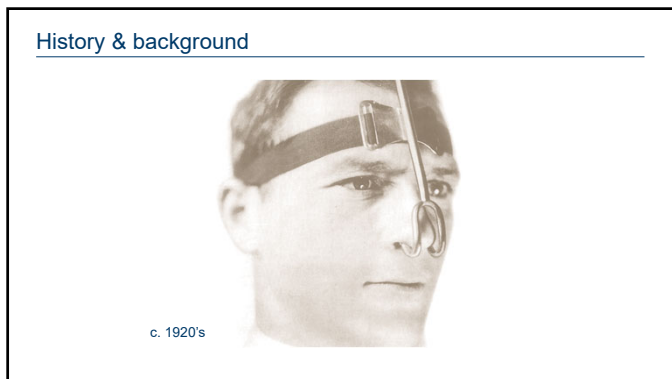
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*Q2: Who routinely used HFNC in their ED
during COVID-19?*

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*Q3: Who understands the physics and
physiology supporting HFNC?*

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History & background

1214 DECEMBER 7, 1968 PRELIMINARY COMMUNICATIONS THE LANCET

tests demonstrated severe delayed hypersensitivity reaction, maximal at 48-72 hours. This response was to the first application after transplant and approximately 3 months after previous tests. It is probable that small amounts of the chemicals remained in the tissues and when thymic function was established, sensitisation occurred. Biopsy of a lymph-node 8 months after implantation of thymic tissue was normal for an infant of this age (fig. 4b). This finding, coupled with normal numbers of circulating lymphocytes, indicated repopulation of peripheral lymphoid tissue with small lymphocytes. After operation

CONTINUOUS CONTROLLED HUMIDIFICATION OF INSPIRED AIR

Summary It has been observed that gases can be administered through the nose at high flow-rates provided that they are at body-temperature and fully saturated with water-vapour. A simple and easily portable system has been devised for delivering gases in this way, and has been shown to be effective in volunteers. It is now proving satisfactory in clinical use, both for continuous humidification and for administration of oxygen.

Department of Anaesthesia, Rigshospitalet, Copenhagen, Denmark

NIELS LOMHOLT M.D. Copenhagen

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History & background

1214 DECEMBER 7, 1968 PRELIMINARY COMMUNICATIONS THE LANCET

Most of the problems of humidification could be solved by the use of water-vapour instead of aerosols. This would more nearly reproduce the physiological mechanism of humidification in the respiratory tract. Such a method became practicable when the author discovered that gases could be blown into one nostril at 20-30 litres per minute without discomfort, and even without perception, provided that the gas was at body-temperature and 100% saturated with water-vapour. (The highest tolerable flow of dry, cool gas is normally regarded as 6-8 litres per minute.)

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AIR

ases can be use at high perature and e and easily ing gases in 1 volunteers. oth for con-n of oxygen.

: LOMHOLT Copenhagen

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High flow fundamentals

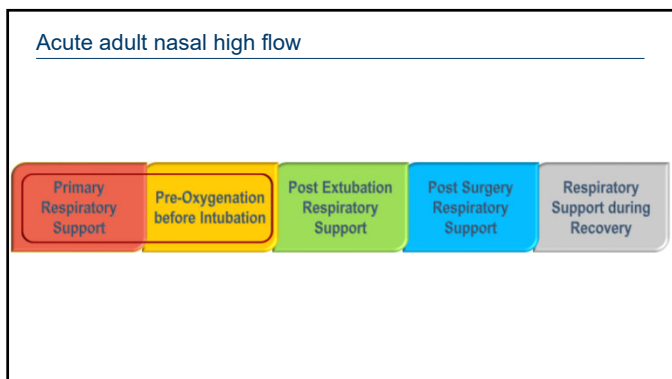
Interface

- High flow nasal cannula (HFNC)
- High flow nasal prongs (HFNP)
- High flow oxygen (HFO)
- Humidified high flow nasal cannula (HHFNC)

Therapy

- High flow therapy (HFT)
- High flow oxygen/therapy (HFO/T)
- Humidified high flow therapy (HHFT)
- Nasal high flow (NHF)
- Optiflow™
- High velocity nasal insufflation (HVNI™)
- Comfort Flo™

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What is nasal high flow?

Nasal high flow therapy is the delivery of heated and humidified air (w/ or w/o supplemental oxygen), up to 60 L/min, to a patient using a high flow nasal cannula (HFNC).

Mechanisms of Action

- Respiratory support
 - Reduction of dead space
 - Dynamic positive airway pressure
- Airway hydration
- Supplemental oxygen
- Patient comfort

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Mechanisms of Action

- Heated humidification of inhaled gas
- Washout of upper airways
- High nasal respiratory flow
- Positive airway pressure
- Entrainment of ambient air

Effects include: Secretion clearance, Dead space reduction, Nasal resistance, Recruitment of atelectatic lung regions, Inspired FIO₂, Metabolic cost of breathing, Minute ventilation requirement, Dynamic compliance, Improving V/Q mismatching, Respiratory rate, Respiratory effort/WOE, Stress and strain (Opening/closure, Stress relievers), Tension-time index, Mechanical power, Expiratory (re)centering diaphragm loading, Comfort and tolerance, Diaphragm load/reducing, VILI, Oxygenation, and Improved Clinical Outcomes.

Illustration by Jeanelle Schaffer Medical Illustration

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Mechanisms of action

Mechanisms of Action

- Respiratory support
 - Reduction of dead space
 - Dynamic positive airway pressure
- Airway hydration
- Supplemental oxygen
- Patient comfort

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Reduction of dead space

REDUCTION OF DEAD SPACE

- Clearance of expired air in the upper airways
- Reduces rebreathing of gas with high CO₂ and depleted O₂
- Increases alveolar ventilation

1. Miller et al. J Appl Physiol 2015

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Reduction of dead space

Modelling of CO₂ in patient airways during nasal high flow therapy with computational fluid dynamics^{1,2}

Airway Modelling
Obtained from CT scan (50 images, 0.6mm space)
Model and cannula at x1.5 scale

End Expiration
Unassisted breathing vs. High NF (40 L/min)

FULL VERSION (4 MINS) **COMPARISON (30 SECS)**

1. Georgehan et al. Exp Fluids 2012
2. Spence et al. Exp Fluids 2012

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Reduction of dead space: Spence

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Reduction of dead space: Moller

Clearance rate related to NHF flow

NHF (L/min)	Clearance rate (mL/d)
15 L/min	~25
30 L/min	~50
45 L/min	~80

Adapted from Moller et al. J Appl Physiol. 2015.

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Reduction of dead space: Moller

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Dynamic positive airway pressure

DYNAMIC POSITIVE AIRWAY PRESSURE

- Breath- and flow-dependent airway pressure^{1,2}
- Promotes slow and deep breathing
- Increases alveolar ventilation¹

Respiratory support

- Reduces work of breathing
- Reduces oxygen requirements
- Reduces risk of hypoxemia
- Reduces risk of hypercapnia
- Reduces risk of respiratory acidosis
- Reduces risk of respiratory arrest

Respiratory support with Nasal High Flow

Unassisted breathing

Respiratory support with Nasal High Flow

AWAY PRESSURE

TIME

INSPIRATION **EXPIRATION**

AWAY PRESSURE

TIME

INSPIRATION **EXPIRATION**

1. Hoshino et al. J Appl Physiol. 2015.
2. Bhatia et al. Respir Care. 2014;59:1022-1028.

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Dynamic positive airway pressure

Respiratory support

- Reduces work of breathing
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Respiratory support with Nasal High Flow

Unassisted breathing

AWAY PRESSURE

TIME

INSPIRATION **EXPIRATION**

Promotes slow, deep breathing

Tidal Volume (V_T)

Control **NHF (45 L/min)**

Adapted from Moller et al.

- Pressure dynamically changes depending on breath and flow
- Inspiratory resistance decreases, making inspiration easier
- Expiratory resistance increases, leading to prolonged expiration

1. Hoshino et al. J Appl Physiol. 2015.
2. Bhatia et al. Respir Care. 2014;59:1022-1028.

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What changes are seen in patients using NHF?

Respiratory support

- Reduces work of breathing
- Reduces oxygen requirements
- Reduces risk of hypoxemia
- Reduces risk of hypercapnia
- Reduces risk of respiratory acidosis
- Reduces risk of respiratory arrest

NHF increases airway pressure, end-expiratory lung volume and tidal volume.¹

1. Bhatia et al. Respir Care. 2014;59:1022-1028.
2. Hoshino et al. J Appl Physiol. 2015.

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Supplemental oxygen

SUPPLEMENTAL OXYGEN WHEN REQUIRED

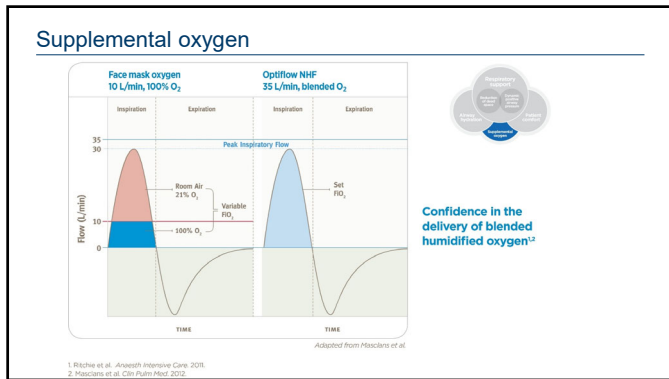
Confidence in the delivery of blended, humidified oxygen¹

Respiratory support

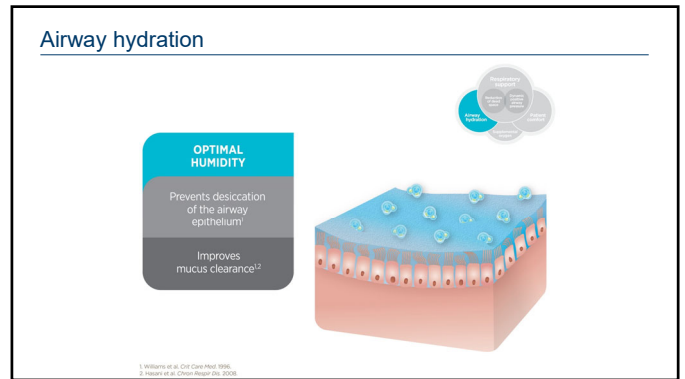
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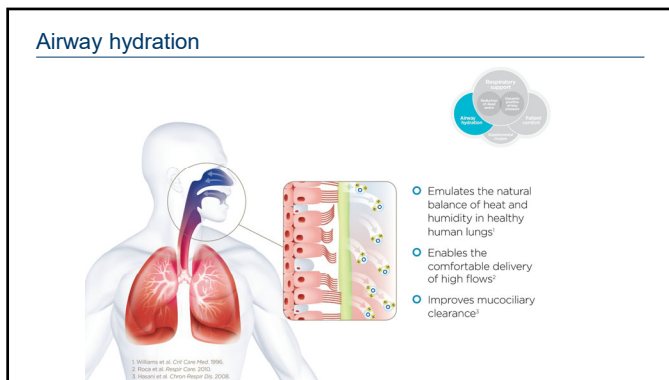
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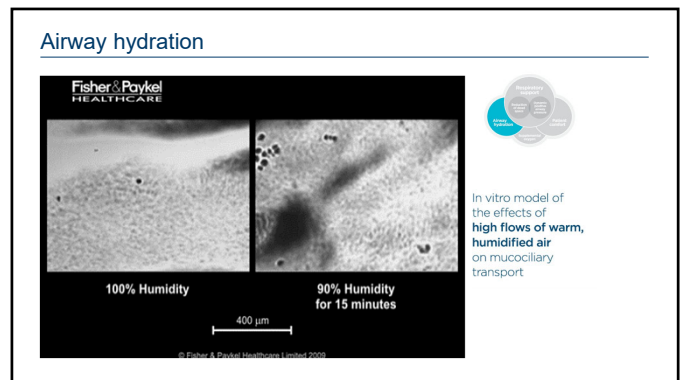
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How important is providing optimal humidity? ▲ COVID-19

- COT delivers dry, unheated gas to patient airways, which can damage cilia and increase thickened secretions (e.g. low flow O₂ cannula, masks and unheated NIV)
- Optimal humidity (37°C, 44 mg/L H₂O) improves mucociliary clearance, which promotes mobilization and thinning of these secretions
- This same mechanism is also crucial across the care continuum with NIV and Invasive therapies
- Evidence has shown that COVID-19 patients develop dry cough and thick respiratory secretions




Image 1 – Healthy Ciliated Epithelium

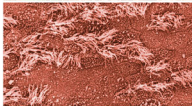
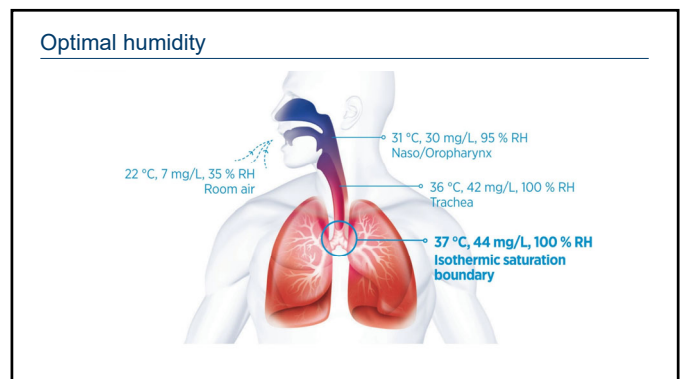


Image 2 – Damaged Ciliated Epithelium

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Water vapor and water droplets

Water vapor molecules can not transport pathogens, which may cause infection, due to their respective size difference

COVID-19

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Patient comfort

COMFORTABLE^{1,2} AND EASY TO USE

OPEN SYSTEM
No seal required

Patient tolerance^{1,3}

COVID-19

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Wide body of evidence supporting nasal high flow

Flow rates used in the 52 controlled studies on acute adult NHF (with subjects n > 39)

A recent systematic search of the PubMed database found 52 acute adult NHF controlled studies.

- 85% reported flow rates above 45 L/min
- 94% reported using F&P Optiflow systems

COVID-19

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What is the clinical evidence specific to the ED?

Nasal high flow can decrease the need for escalation and might decrease the need for intubation

(Meta-analysis; nasal high flow compared with COT and NIV)

- Huang, et al. Emerg Med Int. 2019.

"Patients with HFNC were much more likely to recover from respiratory failure."

(Compared with COT in patients with acute hypoxemic respiratory failure)

- Mace, et al. Am J Emerg Med. 2019.

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Nasal high flow in the ED: clinical studies summary

Flow rate (L/min)	Temp	Population	Reduced escalation	Reduced respiratory rate	Improved oxygenation	Reduced PaCO ₂	Improved comfort	Reduced dyspnea
Huang 2019 (Meta-analysis)	35 - 50		•				•	•
Mace 2019	50 (37 °C)	Acute hypoxemic respiratory failure				•		•
Bell 2018	50 (37 °C)	Unfractionated shortness of breath	•	•				•
Lenglet 2015	40 (37 °C)	Acute respiratory failure				•		•
Jeong 2018	Not reported (37 °C)	Acute hypoxemic respiratory failure (sic: hypoxemic PFS)				•		•
Hakide 2017	35 (37 °C)	Mild to moderate cardiogenic pulmonary edema				•		•
Rittayamai 2018	35 (37 °C)	Acute dyspnea and hypoxemia					•	•

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Evidence based guidelines for clinical mgmt. of COVID-19

Guideline	Nasal High Flow
WHO	May be used in patients with mild ARDS
NIH	Recommended over NIV in patients with AHRF despite COT
SSC*	Suggest use over COT and NIV in patients with AHRF
ANZICS	Considered for patients with hypoxemia

▲ COVID-19

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Evidence based guidelines for clinical mgmt. of COVID-19

Guideline	Systematic Reviews w/ Meta Analyses
WHO	
NIH	Zhao et al. 2017
SSC*	Ou et al. 2017
	Ni et al. 2018
	Rochweg et al. 2019
ANZICS	Agarwal et al. 2020

82% of studies required flows > 45 L/min

▲ COVID-19

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Evidence based guidelines for clinical mgmt. of COVID-19

- **ACEP Respiratory Support for Adult Patients with COVID-19** suggest the use of **high flow nasal oxygen (HFNO)** was associated with lower mortality in hypoxemic respiratory failure. Compared to conventional oxygen therapy, HFNO is associated with decreased risk of subsequent intubation and need for ICU admission.
- **ATS Diagnosis and Management of COVID-19 Disease Guidelines** recommend early use of oxygen by **high-flow nasal cannula (HFNC) in patients requiring more than standard nasal O₂** without indications for immediate intubation.
- **DoD COVID-19 Practice Management Guide** suggest although an area of controversy, early expert opinion favors **high flow nasal cannula (HFNC)** over other non-invasive modalities because it appears to be well tolerated, more efficacious than BIPAP and less provider intensive. There is presently no definitive evidence that HFNC augments transmission of virus.

▲ COVID-19

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When a respiratory compromised patient presents in your ED

<p>If hypoxemic:</p> <p>Low levels of blood oxygen</p> <ul style="list-style-type: none"> • SpO₂ < 92%, ABG: PaO₂ < 75mm Hg <p>Frat. NEJM. 2015.</p> <ul style="list-style-type: none"> • 23 ctr RCT, 310 pts AHRF, NHF vs COT vs NIV • NHF reduced mortality and need for intubation <p>Bell. Emerg Med Aust. 2015.</p> <ul style="list-style-type: none"> • 2 ctr RCT, 100 ED pts with acute undifferentiated shortness of breath, NHF vs COT • NHF reduced escalation in ventilatory support <p>Ischaki. Eur Resp Rev. 2017.</p> <ul style="list-style-type: none"> • Literature review (99 papers) and treatment algorithm <p>Clinical Practice Guidelines</p> <ul style="list-style-type: none"> • ESICM, 2020 – recommend HFNC over COT • ACP, 2021 – use HFNC over NIV • SCCM, 2021 – suggest HFNC over NIV 	<p>If hypercapnic:</p> <p>High partial pressure of blood carbon dioxide</p> <ul style="list-style-type: none"> • PaCO₂ > 45 mmHg, pH < 7.35 <p>Jeong. Am J Emerg Med. 2015.</p> <ul style="list-style-type: none"> • Retrospective ABG analysis of 81 ED pts with ARF • Reduced PaCO₂ and RR in hypercapnic group • Increased PaO₂ and SpO₂ for hypercapnic and non-hypercapnic groups <p>Cortegiani. Crit Care. 2020.</p> <ul style="list-style-type: none"> • 9 ctr RCT, 79 pts AECOPD, NHF vs NIV • NHF non-inferior to NIV as initial ventilatory support • 32% of pts receiving NHF required NIV by 6h <p>Guidance</p> <ul style="list-style-type: none"> • Pantazopoulos. COPD. 2020. • Literature review (9 RCTs) and treatment algorithm • NHF recommended for patients with <ul style="list-style-type: none"> - pH between 7.25 – 7.35 - escalate to NIV for pH < 7.25
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Can the early use of high flow reduce the rate of intubation?

Frat et al. 2015 NEJM
FLORALI Study

REduces mortality rate

REduces escalation of care

STUDY

A 23-center study compared nasal high flow (NHF) therapy to use of a non-rebreather mask and NIV as a primary treatment (pre-intubation).

METHOD

- 310 patients in acute hypoxemic respiratory failure (PaO₂/FiO₂ ≤ 300 mmHg) were randomized to receive NHF, non-rebreather mask or NIV.
- Primary outcome number of patients intubated at day 28 - not atbared.

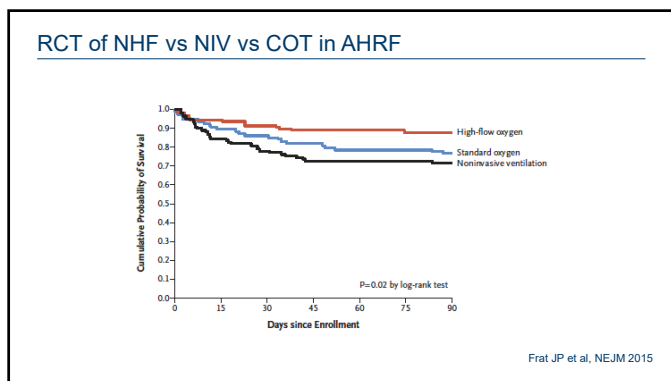
RESULTS

- ▶ NHF significantly reduced ICU mortality: NHF 11%, standard O₂ therapy 19%, NIV 25% and 90-day mortality: NHF 12%, standard O₂ therapy 23%, NIV 28%
- ▶ NHF significantly reduced need for intubation in more acute patients (PaO₂/FiO₂ ≤ 200 mmHg)
- ▶ Significant increase in ventilator-free days on NHF
- ▶ NHF significantly reduced intensity of respiratory discomfort and dyspnea

39% fewer intubations between NIV and NHF

Primary Respiratory Support

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Bell et al. 2015 Emergency Medicine Australasia

REDUCED respiratory rate

REDUCED escalation

IMPROVED patient comfort

STUDY

A comparison of NHF with conventional oxygen therapy (COT) in patients with acute undifferentiated shortness of breath in the ED

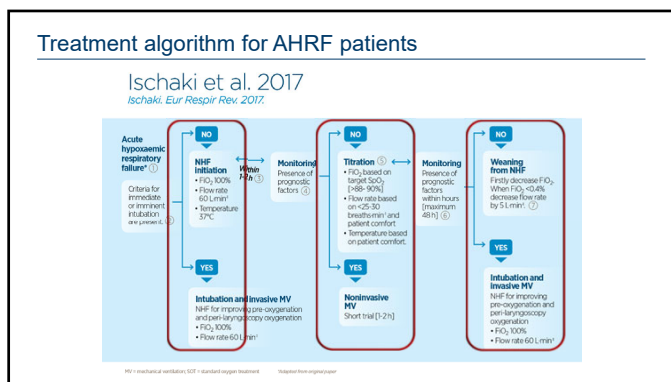
METHOD

- Randomized controlled trial in two Australian EDs
- 100 patients with undifferentiated shortness of breath
- NHF flow rate was commenced at 50 L/min with FiO₂ at 30%
- Primary outcomes: The need to escalate ventilation therapy or a reduction in respiratory rate of 20% or more within 2 hours

RESULTS

- Significantly reduced escalation in ventilatory support using NHF (4.2% NHF vs 19% COT, p = 0.02)
- Higher proportion of patients had > 20% reduction in respiratory rate using NHF (66.7% NHF vs 38.5% COT), p = 0.005
- More patients demonstrated a reduction in dyspnea (Modified Borg score: 75% NHF vs 55.8% COT), p = 0.044
- Significant increase in patient comfort with NHF (Numerical scale out of 5 (very comfortable): 4 (NHF) vs 3 (COT), p = 0.035)

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- ESICM, 2020 – recommend HFNC over COT
- ACP, 2021 – use HFNC over NIV
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If hypercapnic:

High partial pressure of blood carbon dioxide

- PaCO₂ > 45 mmHg, pH < 7.35

Jeong, Am J Emerg Med. 2015.

- Retrospective ABG analysis of 81 ED pts with ARF
- Reduced PaCO₂ and RR in hypercapnic group
- Increased PaO₂ and SpO₂ for hypercapnic and non-hypercapnic groups

Cortegiani, Crit Care. 2020.

- 9 ctr RCT, 79 pts AECOPD, NHF vs NIV
- NHF non-inferior to NIV as initial ventilatory support
- 32% of pts receiving NHF required NIV by 6h

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Clinical Practice Guidelines for hypoxemic patients

icm

The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline.

Rochewig B, et al. 2020

"We recommend using HFNC compared to COT for patients with acute hypoxemic respiratory failure."

ACP

Appropriate use of high flow nasal oxygen in hospitalized patients for initial or postextubation management of acute respiratory failure: A clinical guideline.

Gaesein A, et al 2021

"Use high-flow nasal oxygen rather than noninvasive ventilation in hospitalized adults for the management of acute hypoxemic respiratory failure."

Society of Critical Care Medicine

Surviving Sepsis Campaign, 2021: international guidelines for management of sepsis and septic shock

Grave L, et al 2021

"For adults with sepsis-induced hypoxemic respiratory failure, we suggest the use of high flow nasal oxygen over noninvasive ventilation."

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Jeong et al. 2015 American Journal of Emergency Medicine

REduced respiratory rate

REduced PaCO₂

IMPROVES oxygenation

STUDY

A retrospective analysis of arterial blood gases (ABG) of patients treated with NHF with respiratory failure, with and without hypercapnia in the ED

METHOD

- 81 (46 hypercapnic) patients with acute respiratory failure
- NHF flow rate and FiO₂ determined at physician's discretion
- Primary outcome: change in Arterial Blood Gas (ABG)

RESULTS

- Significant reduction in PaCO₂ in the hypercapnic group: 73.2 mmHg ± 20.0 to 67.2 mmHg ± 23.4, p = 0.02
- Significant increase in PaO₂ and SpO₂ for hypercapnic and nonhypercapnic patients: overall 64.7 mmHg ± 33.3 to 80.0 mmHg ± 31.4, p < 0.01; overall 83.3% ± 14.4 to 92.0% ± 7.3, p < 0.01
- Significant reduction in respiratory rate for patients with hypercapnia: 24.7 breaths per minute ± 5.8 to 23.6 ± 5.2, p = 0.03

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Cortegiani et al. 2020 Critical Care

High flow nasal therapy versus noninvasive ventilation as initial ventilatory strategy in COPD exacerbation: a multicenter non-inferiority randomized trial.

Design

9 centered RCT

Patients

n = 79
Mild-to-moderate AECOPD (pH 7.25-7.35, PaCO₂ ≥ 55 mmHg before ventilator support)

Intervention	Control
NHF	NIV

Outcome

Primary: PaCO₂ from baseline to 2 h (non-inferiority margin 10 mmHg)
Secondary: non-inferiority of NHF to NIV in reducing PaCO₂ at 6 h rate of treatment changes, dyspnea, discomfort, RR, ABG, hospital LoS, mortality

Results

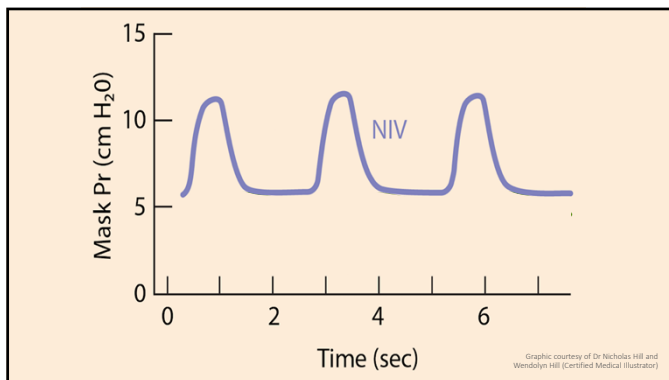
Mean PaCO₂ reduction from baseline at 2 hours

p = 0.404

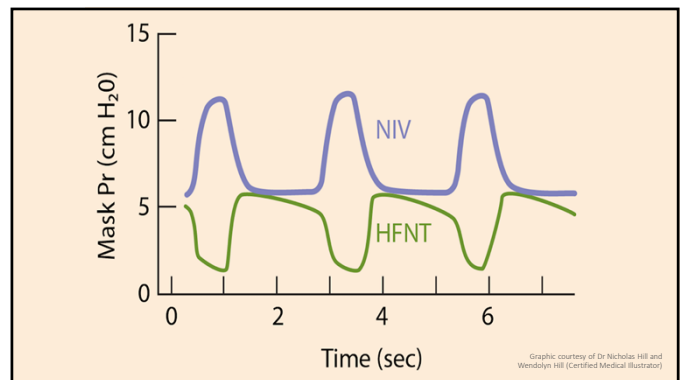
Group	Mean PaCO ₂ reduction (mmHg)
NIV	9.5
NHF	6.8

- NHF was non-inferior to NIV in reduction of PaCO₂ (p = 0.0003).
- Both treatments had a significant effect on PaCO₂ reductions over time, and trends were similar between groups.
- 32% of NHF patients required NIV by 6 h.

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Pantazopoulos et al. 2020 COPD: Journal of Chronic Obstructive Pulmonary Disease

Nasal high flow use in COPD patients with hypercapnic respiratory failure: treatment algorithm & literature review

Design

Literature review

Aim

Discuss suitability of NHF therapy for COPD patients who cannot tolerate NIV and propose a therapy algorithm for patients with AECOPD based on current literature.

Search result

AECOPD (9 studies)

PANTAZOPOULOS ET AL. 2020 COPD: Journal of Chronic Obstructive Pulmonary Disease

Conclusions

NHF may be used in place of NIV in least tolerate and compliant patients, or in association with NIV to reduce mask-related side effects.

Takeaway

NHF recommended as initial ventilatory support for patients with:

- pH between 7.25 – 7.35
- PaCO₂ ≥ 45 mmHg
- Escalate to NIV for pH < 7.25

Consider NHF as an initial ventilatory strategy

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Guidance for hypercapnic patients

CLINICAL EVIDENCE FOR USE IN AECOPD

Study	Improved pH	Improved PaCO ₂	Non-inferior to NIV	More comfortable**
Cortegiani et al. 2020	•	•	•	•
Branchett et al. 2018	•	•	•	•
Kim et al. 2018	•	•	•	•
Yokoi et al. 2019	•	•	•	•
Pfeifer et al. 2017	•	•	•	•
Lee et al. 2018	•	•	•	•
Oh et al. 2020	•	•	•	•

PANTAZOPOULOS ET AL. 2020 COPD: Journal of Chronic Obstructive Pulmonary Disease

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When a respiratory compromised patient presents in your ED

If hypoxemic:

- Low levels of blood oxygen
- SpO₂ < 92%, ABG: PaO₂ < 75mm Hg

If hypercapnic:

- High partial pressure of blood carbon dioxide
- PaCO₂ > 45 mmHg, pH < 7.35

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What flow rates and ranges are used?

Guidance source	Category description	Flow L/min
Hernandez et al Oct 2016	established patients at high risk of reintubation*	~55
Hernandez et al Apr 2016	established patients at low risk of reintubation*	~35
Elli et al 2015	acute undifferentiated shortness of breath in the ED†	~35
Frost et al 2015	acute hypoxemic respiratory failure (pre-intubation)†	~45
Stephan et al 2015	hypoxemic patients post cardiothoracic surgery†	~45
Maggiore et al 2014	post intubation with acute respiratory failure†	~45
Peters et al 2012	do not intubate patient with hypoxemic respiratory distress†	~45
Sztrymf et al 2011	acute respiratory failure†	~45
Parke et al 2011	mild-to-moderate hypoxemic respiratory failure†	~45
Conroy et al 2011	post-cardiac surgery†	~45
Criso et al 2016	stable severe COPD patients†	~45
Fine et al 2010	COPD, bronchiectasis†	~45
Hessari et al 2008	bronchiectasis†	~45

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How much pressure is generated?

Pressure increases approximately 0.5 – 1 cmH₂O per 10 L/min of flow¹⁻³

For example, flows of 50 L/min generate 2.5 – 5.0 cm H₂O

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When are the effects of nasal high flow observed?

- Respiratory rate: 5 minutes¹ – 15 minutes²
- Oxygenation: 10 minutes² – 15 minutes³
- Dyspnea: 5 minutes⁴ – 30 minutes⁵
- Supraclavicular retraction: 30 minutes⁶
- Thoracoabdominal asynchrony: 30 minutes⁶

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How do we know if nasal high flow will be successful?

First look at the ROX index: defined by three common noninvasive measurements:

$$\frac{SpO_2 / FiO_2}{RR} = ROX \text{ index}$$

Roca & colleagues conducted derivation (2016) and validation (2019) studies of the ROX index to predict the success of HFNC in pneumonia patients with AHRF

Oxygen saturation measured by SpO₂ / FiO₂ had a greater weight than RR

SpO ₂ / FiO ₂	Respiratory rate	ROX index
95/0.21	15	30.2
95/0.85	37	3.0

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Using the ROX index to predict the outcome of Nasal High Flow

"The authors confirmed that a ROX value of ≥ 4.88 predicted the success of NHF"

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EPIC flowsheet

HF Nasal Therapy		HF Nasal Therapy	
Charges		Equipment Details	
Oxygen Need and Devices		Respiratory Assessment	
Respiratory Vitals		Comfort Evaluation	

Courtesy of UnityPoint Health, Des Moines, IA

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- ### Review
- 1 What are the origins of HFNC?
 - 2 What are the mechanisms of action?
 - 3 How can high flow be used effectively in your ED? ▲ COVID-19
 - 4 Q & A

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Any volunteers to experience nasal high flow?

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Thank you from Fisher & Paykel Healthcare
Open for any questions

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