Intensive Care Med
https://doi.org/10.1007/s00134-024-07386-8

EDITORIAL

High-flow nasal cannula: evolving practices and novel clinical and physiological insights

Oriol Roca[1,2,3*], Jie Li[4] and Tommaso Mauri[5,6]

Latest advances in understanding the physiological effects of high-flow nasal cannula

High-flow nasal cannula (HFNC) systems deliver heated and humidified gases, usually at 30–60 L/min, at a set desired fraction of inspired oxygen (FiO_2) [1]. This, in turn, improves carbon dioxide (CO_2) clearance and, by exceeding peak tidal inspiratory flows, achieves more stable alveolar oxygen fractions, as less room-air is entrained [2]. After accounting for some modifying factors (e.g. mouth closed), HFNC can generate a variable low positive end-expiratory pressure [3, 4]. These physiological effects are proportional to the set flow rate and benefit critically ill patients with respiratory diseases by reducing respiratory drive, inspiratory effort and minute ventilation [4] (Fig. 1).

Beyond flow selection, recent findings highlight the physiological relevance of HFNC interface, body position and respiratory rate. Asymmetrical prongs applied to hypoxemic patients supported by conventional HFNC were shown to improve CO_2 clearance, determining a 19.6% reduction of minute ventilation compared to classical cannulas [5]. HFNC combined with awake-prone positioning moves end-expiratory transpulmonary pressure closer to 0 cmH_2O and reduces dynamic lung strain [6]. Finally, the efficiency of CO_2 washout by HFNC decreases at higher respiratory rate, especially with flow < 60 L/min, while asymmetrical cannula interface could limit this phenomenon [7].

HFNC in acute hypoxemic respiratory failure

HFNC may be indicated for all hypoxemic patients who do not improve oxygenation or experience relief from respiratory distress when using conventional oxygen therapy, given the absence of contraindication. In these patients, HFNC has been shown to reduce intubation rates without affecting mortality [1]. Similarly, it can be used as a post-extubation supportive therapy, decreasing the need for reintubation when non-invasive ventilation (NIV) is not indicated. Indeed, in the post-extubation period, HFNC may be equivalent to NIV in some clinical scenarios. In patients with acute hypoxemic respiratory failure (AHRF), HFNC could be started with an initial flow of 30–40 L/min and rapidly escalated to the maximum tolerated. Conversely, in post-extubation, HFNC may be initiated with slightly lower flows, with subsequent titration upwards in a manner akin to AHRF patients, albeit with a modest reduction in the maximum tolerated flow. The differences in peak inspiratory flow generated may explain these variations [2]. In AHRF or post-extubation, FiO_2 should be titrated according to the oxygenation values. Finally, HFNC temperature significantly influences patient comfort. Ideally, the gas should be delivered at 37 °C. However, lower temperatures may be associated with better comfort [8] (Fig. 1).

One notable advantage of HFNC lies in its enhanced patient comfort compared to other non-invasive respiratory support therapies, allowing for continuous administration 24 h per day. Despite conceptualised optimal settings and the inherent heterogeneity in HFNC effects among patients, prioritising patient tolerance remains paramount.

HFNC in acute and chronic hypercapnic respiratory failure

In recent years, HFNC has been increasingly utilised to treat patients with hypercapnic respiratory failure across

*Correspondence: oroca@tauli.cat
[1] Servei de Medicina Intensiva, Parc Taulí Hospital Universitari, Institut d'Investigació i Innovació Parc Taulí (I3PT-CERCA), Institut de Recerca Part Taulí–I3PT, Parc del Taulí 1, 08028 Sabadell, Spain
Full author information is available at the end of the article

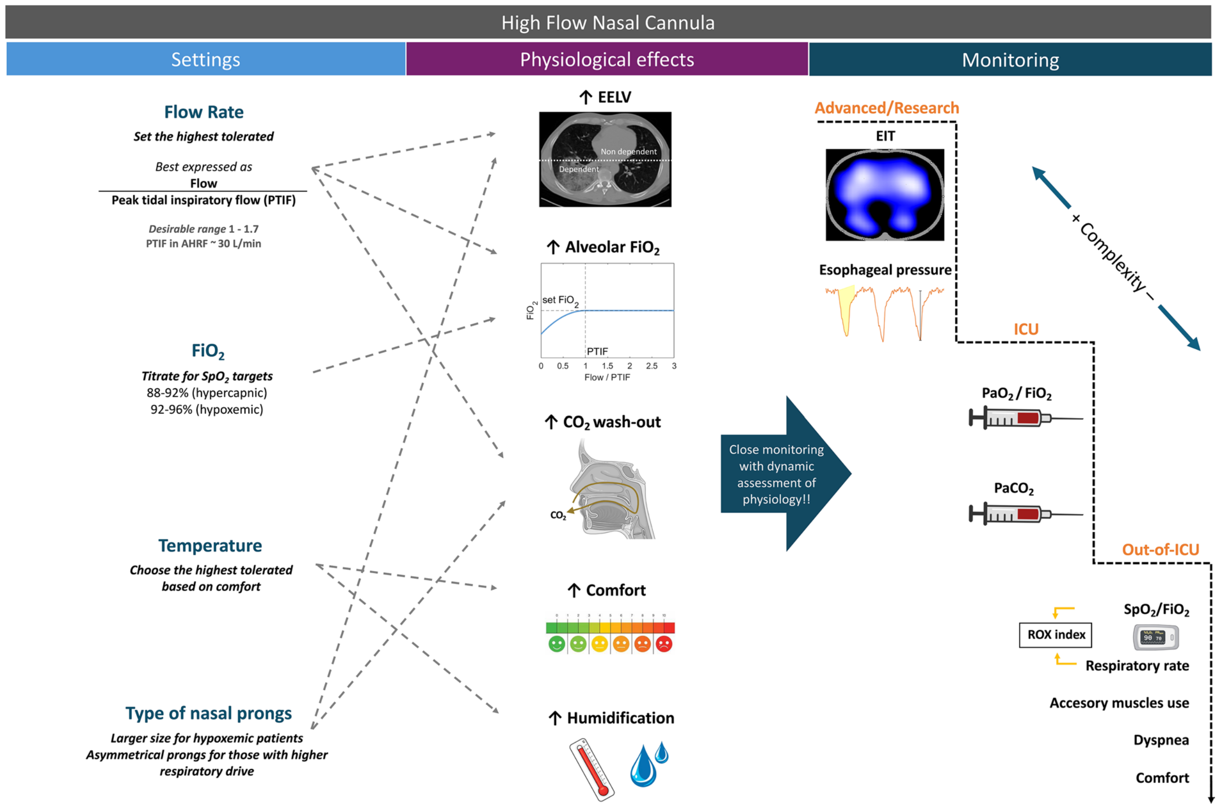

Fig. 1 Multidimensional approach to the settings and monitoring of high-flow nasal cannula (HFNC) therapy for patients with acute respiratory failure. AHRF: Acute hypoxemic respiratory failure; EELV: end-expiratory lung volume; FiO_2: fraction of inspired oxygen; CO_2: carbon dioxide; EIT: electrical impedance tomogrpahy; PaO_2: partial pressure of oxygen in arterial blood; $PaCO_2$: partial pressure of carbon dioxide in arterial blood; SpO_2: pulse oximetry

various conditions. Our updated meta-analysis reaffirmed previous findings when HFNC was employed as the initial treatment for acute hypercapnic respiratory failure [9], indicating no significant differences in the intubation risk between HFNC and NIV, (supplemental Fig. S1, Table S1). Two randomised controlled trials (RCTs) involving patients with chronic obstructive pulmonary disease (COPD) and mild hypercapnia (defined as pH ≥ 7.35 and $PaCO_2$ > 45 mmHg) demonstrated very low and comparable intubation rates between HFNC and conventional oxygen therapy [10]. However, Xia et al. [11] reported prolonged hospital stays in patients with high bicarbonate treated with HFNC, attributing it to delayed NIV escalation. Limited sample sizes in both study sets hinder robust conclusions, necessitating further RCTs.

Although NIV remains the first-line technique for managing hypercapnia in COPD exacerbations, HFNC can be considered between NIV sessions or in cases of NIV intolerance in patients with mild-to-moderate hypercapnia. In these patients, adequate CO_2 clearance may be achieved with lower flows (30 L/min) compared to hypoxemic patients, and the FiO_2 should be titrated according to the oxygenation target, which is lower than in hypoxemic patients. Following extubation in patients with hypercapnic respiratory failure, our updated meta-analysis showed no significant differences in the risk of re-intubation between HFNC and NIV (Fig. S2). However, until further evidence is available, NIV remains the first-line therapy. Lastly, for stable hypercapnic COPD patients requiring long-term oxygen therapy at home, a recent RCT reported lower rates of moderate/severe exacerbations in the HFNC group compared to conventional oxygen therapy [12].

The importance of detecting HFNC failure

Delayed intubation in patients treated with HFNC has been consistently associated with worse outcomes [13]. Therefore, investigating the determinants of HFNC failure is imperative. However, there is no consensus regarding the specific threshold of physiological variables that trigger intubation. Therefore, the decision to intubate is ultimately based on the physician's clinical judgement at the bedside.

The progression of respiratory failure remains the principal reason for intubation in HFNC patients, and it has been hypothesised that this may be related to the inability to mitigate patient self-inflicted lung injury through the physiological benefits provided by HFNC [14]. However, routine clinical practice rarely involves monitoring inspiratory effort or transpulmonary pressures during HFNC treatment. Consequently, bedside clinical assessment is crucial to identify HFNC failure. Several variables, including lack of improvement in oxygenation or reduction in respiratory rate following the initiation of HFNC, presence of thoracoabdominal asynchrony, and increased systemic severity, indicate HFNC failure. Furthermore, the ROX index (defined as the ratio of oxygen saturation as measured by pulse oximetry/FiO_2 to respiratory rate)—which calculates the ratio of SpO_2/FiO_2 to respiratory rate—has demonstrated superior predictive diagnostic accuracy compared to assessing these variables individually [15] (Fig. 1). A RCT is ongoing to explore whether using ROX as a criterion for intubation would decrease the time to intubation in patients who fail HFNC (NCT04707729).

HFNC weaning

Given its non-invasive nature, HFNC can be easily removed and resumed, making weaning HFNC in adult patients less of a concern. Many RCTs investigating HFNC lack specific weaning criteria, though some suggest discontinuation or switching to conventional oxygen if patients are stable with respiratory rates ≤ 25 breaths/min and $SpO_2 \geq 92\%$, at the settings of flow 30 L/min and FiO_2 0.4 (Table S2). In a retrospective analysis of 190 HFNC-treated patients, an $FiO_2 \leq 0.4$ and a $ROX \geq 9.2$ were identified as predictors of HFNC weaning success [16]. However, the sequence of reducing HFNC variable (flow or FiO_2) remains to be investigated, a general consensus leans towards weaning FiO_2 to 0.4, if tolerated, reducing flow to 30 L/min.

Take-home message

Offering benefits such as improved oxygenation and CO_2 clearance, reduced respiratory drive, and enhanced patient comfort, HFNC has reshaped the approach to non-invasive respiratory support. Despite its advantages, the need for close monitoring and an individualised approach to therapy is paramount, as delayed intubation in HFNC-treated patients can lead to adverse outcomes. Future research focusing on refining weaning protocols, adjusting therapy variables, and understanding patient-specific responses is essential to fully harness the potential of HFNC.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1007/s00134-024-07386-8.

Author details

[1] Servei de Medicina Intensiva, Parc Taulí Hospital Universitari, Institut d'Investigació i Innovació Parc Taulí (I3PT-CERCA), Institut de Recerca Part Taulí–I3PT, Parc del Taulí 1, 08028 Sabadell, Spain. [2] Departament de Medicina, Universitat Autònoma de Barcelona, Bellaterra, Spain. [3] Ciber Enfermedades Respiratorias (Ciberes), Instituto de Salud Carlos III, Madrid, Spain. [4] Division of Respiratory Care, Department of Cardiopulmonary Sciences, Rush University, 600 S Paulina St, Suite 765, Chicago, IL 60612, USA. [5] Department of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. [6] Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy.

Declarations

Conflicts of interest

OR reports receiving a research grant from Hamilton Medical AG and Fisher & Paykel Healthcare Ltd, speaker fees from Hamilton Medical AG, Fisher & Paykel Healthcare Ltd, Aerogen Ltd, and non-financial research support from Timpel, and he is a minority shareholder of Tesai Care SL; all outside the submitted work. JL has received research funding from Fisher & Paykel Healthcare Ltd, Aerogen Ltd, American Association for Respiratory Care, and Rice Foundation, and speaker fees from American Association for Respiratory Care, Aerogen Ltd, Heyer Ltd, Vincent Ltd, and Fisher & Paykel Healthcare Ltd. JL is also the section editor of Respiratory Care. TM received speaker fees from Fisher and Paykel, Drager, Telesair, all outside the submitted work.

Received: 29 January 2024 Accepted: 6 March 2024
Published online: 04 April 2024

References

1. Rochwerg B, Einav S, Chaudhuri D et al (2020) The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. Intensive Care Med 46:2226–2237
2. Li J, Albuainain FA, Tan W et al (2023) The effects of flow settings during high-flow nasal cannula support for adult subjects: a systematic review. Crit Care 27:78
3. Parke RL, Bloch A, McGuinness SP (2015) Effect of very-high-flow nasal therapy on airway pressure and end-expiratory lung impedance in healthy volunteers. Respir Care 60:1397–1403
4. Mauri T, Turrini C, Eronia N et al (2017) Physiologic effects of high-flow nasal cannula in acute hypoxemic respiratory failure. Am J Respir Crit Care Med 195:1207–1215
5. Slobod D, Spinelli E, Crotti S et al (2023) Effects of an asymmetrical high flow nasal cannula interface in hypoxemic patients. Crit Care 27:145
6. Grieco DL, Delle Cese L, Menga LS et al (2023) Physiological effects of awake prone position in acute hypoxemic respiratory failure. Crit Care 27:315
7. Tatkov S, Rees M, Gulley A et al (2023) Asymmetrical nasal high flow ventilation improves clearance of CO(2) from the anatomical dead space and increases positive airway pressure. J Appl Physiol 134:365–377
8. Mauri T, Galazzi A, Binda F et al (2018) Impact of flow and temperature on patient comfort during respiratory support by high-flow nasal cannula. Crit Care 22:120
9. Ovtcharenko N, Ho E, Alhazzani W et al (2022) High-flow nasal cannula versus non-invasive ventilation for acute hypercapnic respiratory failure in adults: a systematic review and meta-analysis of randomized trials. Crit Care 26:348

10. Yang H, Huang D, Luo J et al (2023) The use of high-flow nasal cannula in patients with chronic obstructive pulmonary disease under exacerbation and stable phases: a systematic review and meta-analysis. Heart Lung 60:116–126
11. Xia J, Gu S, Lei W et al (2022) High-flow nasal cannula versus conventional oxygen therapy in acute COPD exacerbation with mild hypercapnia: a multicenter randomized controlled trial. Crit Care 26:109
12. Nagata K, Horie T, Chohnabayashi N et al (2022) Home high-flow nasal cannula oxygen therapy for stable hypercapnic COPD: a randomized clinical trial. Am J Respir Crit Care Med 206:1326–1335
13. Kang BJ, Koh Y, Lim CM et al (2015) Failure of high-flow nasal cannula therapy may delay intubation and increase mortality. Intensive Care Med 41:623–632
14. Grieco DL, Maggiore SM, Roca O et al (2021) Non-invasive ventilatory support and high-flow nasal oxygen as first-line treatment of acute hypoxemic respiratory failure and ARDS. Intensive Care Med 47:851–866
15. Roca O, Caralt B, Messika J et al (2019) An index combining respiratory rate and oxygenation to predict outcome of nasal high-flow therapy. Am J Respir Crit Care Med 199:1368–1376
16. Rodriguez M, Thille AW, Boissier F et al (2019) Predictors of successful separation from high-flow nasal oxygen therapy in patients with acute respiratory failure: a retrospective monocenter study. Ann Intensive Care 9:101