

High-flow nasal oxygen therapy in acute respiratory failure

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Abstract

High-flow nasal cannula (HFNC) is a new effective device, which is able to deliver oxygen-therapy at a reliable FiO_2 but also a certain amount of respiratory assistance; however HFNC could not be defined as a *mechanical ventilator*. The main physiologic advantage as compared to conventional oxygen therapy (COT) is the capability of HFNC to meet the increased ventilator demand in patients with respiratory distress and therefore reduce the amount of respiratory muscle's workload. The main clinical advantage over both COT and noninvasive ventilation (NIV) is the greater comfort and acceptability reported by patients. So far there are several indications for HFNC use both in and outside ICU especially for milder hypoxemic spontaneously breathing patients and prevention of extubation failure in intubated patients, as well as palliative care in end stage neoplastic and non-neoplastic respiratory diseases. A large proportion of potential HFNC candidates belongs to advanced age people. Caution should be taken in the selection of the patients, monitoring, escalating treatment and setting of application.

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A part from the clinical conditions which require an immediate ventilator support, conventional oxygen therapy (COT) via a facemask or nasal cannula is considered the *first-step approach* in the escalating therapy for the management of acute respiratory failure (ARF) to *buy the time* for the etiologic therapy to reverse the triggering cause of the acute decompensation.¹ If COT is not enough to properly and quickly correct the impaired lung gas exchange and to reduce the burden of respiratory distress, noninvasive ventilation (NIV) becomes the following option whose aim is to avoid the need for invasive mechanical ventilation (IMV), as well as to prevent its life-threatening complications.² Conversely, when an

intubated and invasively ventilated patient is ready to be extubated, the transition from the assisted mechanically to the spontaneous breathing on COT may be facilitated by the application of NIV especially in subjects with underlying chronic cardio-pulmonary diseases.²⁻⁴ Outside the *do-not intubate (DNI) setting*, the failure of noninvasive strategies (COT and NIV) for escalating and de-escalating pathway leads to a mandatory IMV via respectively endotracheal intubation or re-intubation.^{3,4} Even though in the last two decades NIV has dramatically changed the epidemiology of mechanical ventilation in an expanding number of acute clinical scenarios, the chance of success with this ventilatory technique is variable and strongly dependent on several variables, such as team's experience, patient-ventilator synchrony, non-intentional air leaks, sensorium level, patient's cooperation, adequate equipment and environment, patho-physiology pattern, timing and severity of ARF.³⁻⁵ NIV failure may occur in up to 60% of cases in specific categories of patients, such as hypoxemia de novo, poor interface acceptance, severe altered consciousness, incapability of self-managing a burden of secretions, concomitant non-pulmonary organs dysfunction.⁶ Very recently, similarly to the risk of developing ventilator-induced lung injury (VILI) during IMV applied outside a *protective ventilator strategy*, *NIV-induced lung injury* has been postulated as a mechanism of treatment failure strictly in patients ventilated at higher values of tidal value (*i.e.* >9 mL/kg).^{4,6} Above all, the adherence to the scheduled ventilatory treatment is the crucial *ingredient* for successfully adapting, carrying on and weaning from the ventilator the patient submitted to NIV.²⁻⁵ As a matter of fact, when NIV is likely to fail, physicians may choose to keep on COT both the patients who are still in the early stages of ARF when IMV is not still mandatory, and those who have been successfully weaned from IMV without signs of post-extubation respiratory distress.

Unfortunately, COT has several drawbacks: i) limited amount of oxygen supplied with a maximum flow of 15 L/min; ii) imprecision and instability of the delivered fraction of inspired O_2 (FiO_2) depending on the variability of the patient's breathing pattern; iii) risk of CO_2 -rebreathing with *reservoir* devices; iv) poor subject's mask tolerance especially for long-term treatment, and interference with eating, drinking, speaking; v) insufficient heating and humidification of the administered dry gas; vi) substantial mismatch between the oxygen flow and the patient's inspiratory demand. Concerning the latter, given the fact that the

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patient's peak inspiratory demand may vary between 30 and 120 L/min during an attack of ARF, only a small amount of the inspired gas (*i.e.* below 10%) can be properly humidified and oxygenated.^{1,7,8} Thus may result in severe mucosal damage and impairment of the physiological mechanisms of muco-ciliary clearance.⁷ Finally, COT is unable of unloading the huge work of respiratory muscles⁸ and may, on the other hand, contribute to a rise in $PaCO_2$ level with a contextual drop in pH and the risk of precipitating the need for mechanical ventilation particularly in patients with acute on-chronic hypercapnic respiratory failure.⁸

Recently an alternative system to deliver oxygen therapy has received growing attention in the clinical practice due to its technical properties capable of potentially overcoming the intrinsic limitations of COT devices for the treatment of severely hypoxemic ARF patients who do not still require an immediate ventilator support. High-flow nasal oxygen cannula (HFNC) is a new technological system that can deliver up to 100% heated and humidified oxygen at a maximum flow of 60 L/min of gas via nasal prong or cannula; moreover, it is provided with an air-oxygen blender that allows the administration of gas with a pre-set FiO_2 ranging from 21% to 100%.⁹

When compared to COT, HFNC has several theoretical physiological advantages (Figure 1): i) chance of delivering higher levels of FiO_2 with good reliability; ii) washing-out of the pharyngeal dead space with improved CO_2 clearance; iii) efficient humidification and heating of the delivered oxygen-air mixture with a prevention of

dryness-induced mucosal and muco-ciliary damage and a facilitation of secretion removal; iv) good patient's acceptance without interference with eating, drinking, speaking; v) possibility of matching the HFNC flow rate to the patient's inspiratory demand and/or degree of respiratory distress; vi) generation of a flow-dependent positive expiratory pressure (up to a median of 7.4 cmH₂O at 60 L/min) with a contextual upper airway resistance reduction (*stenting effect*) and, alveolar recruitment (*PEEP-effect*).⁹⁻¹³ Thanks to its favorable actions on respiratory work and its high degree of acceptability, HFNC provides an increased level of respiratory support in comparison with COT devices and has been proposed as a potential alternative respiratory support to NIV, included in geriatric patients, when mechanical ventilation is not mandatory both to prevent the endotracheal intubation and to facilitate the weaning from IMV. Furthermore, the possibility of keeping the high-flow oxygen supplementation in the patients who are going to be intubated or reintubated is another point in favor of HFNC in terms of the safety management of critically hypoxemic patients.⁹

The first study that has pushed forward the role of HFNC in the management of critically ill patients is the prospective, randomized, controlled multicentre French trial performed by Frat *et al.*¹⁴ including 310 patients with hypoxaemic ARF (PaO₂=FIO₂ ratio), predominantly because of pneumonia. Patients were randomized to receive COT, HFNO or NIV. The strengths of this study rely on the well-matched baseline

characteristics of the three groups, the randomization within three hours after the patient's eligibility, the well-defined pre-established criteria for intubation, the exclusion of patients with associated hypercapnia or a history of chronic respiratory failure, as well as those with acute cardiogenic pulmonary oedema or severe neutropenia. The rate of ETI (primary endpoint) was lower among patients treated with HFNO than among those receiving COT or NIV (38% vs 47% and 50%, respectively), but these differences did not achieve statistical significance (P=0.18). In a post hoc analysis including 238 patients who on enrolment had severe hypoxaemia, as defined by PaO₂=FIO₂ ratio <200, intubation turned out to be less likely to occur in the HFNO group than in the two other groups (P=0.009). HFNO significantly improved two secondary outcomes, the ventilator-free days at day 28 and 90 day mortality, compared with both COT (P=0.046) and NIV (P=0.006). The reason why HFNO reduced 90-day mortality is not entirely clear. As tidal volumes on average exceeded 9 mL kg⁻¹ of predicted body weight, the authors hypothesize an increased risk of ventilator-induced lung injury with NIV.

Several methanalysis and systemic reviews have shown that HFNC is better than COT in terms of need of ETI and of escalating treatment (NIV and IMV) even if without a proved advantage in terms of hospital mortality; on the other hand, HFNC seems not to be inferior to NIV for what the main explored outcomes concern (ETI, mortality). It should be considered that

these methanalysis included heterogeneous studies for type and severity of patients. The most convincing data in favor of HFNC have been accumulated for the prevention of post-estubation failure, as HFNC turns out to be more effective than COT in *low-risk* patients and not inferior to NIV in *high-risk* patients.^{9,10} Moreover, an increasing amount of clinical data, even if mostly uncontrolled, are accumulating about the feasibility, efficacy and tolerance of HFNC in hypoxemic ARF of different etiology with the aims of reducing the escalating ventilatory therapy (*i.e.* NIV and IMV), in *DNI patients* as alternative to NIV, in end-stage chronic cardio-pulmonary diseases with ARF, in post-cardiac surgery patients as prophylactic support to reduce the need of mechanical ventilation, during bronchoscopy in high-risk ARF patients.¹³⁻¹⁹ Very recently, HFNC has been shown to achieve some of the physiologic goals of MV also in hypercapnic respiratory failure due to stable COPD (*i.e.* reduction of work of breathing);²⁰ moreover, some experiences demonstrated the capability of HFNC to successfully improve moderate respiratory acidosis in COPD exacerbations.²¹ Thanks to its easier handling and greater patient comfort, so far some on-going RCT are exploring the role of HFNC in acute hypercapnic moderate acidosis as alternative of NIV. Finally, HFNC could be applied not only as alternative to NIV but as an integrative option to be used in the window-time free of the intermittent scheduled NIV in order to get the best synergistic effects from these two noninvasive respiratory devices.

As a matter of the fact, HFNC is a feasible non-invasive respiratory assistance tool that could be applied both in ICU and non-setting depending on the severity of the patients and the risk of escalating therapy (*i.e.*, NIV and IMV). This is particularly true for elderly fragile patients for whom a noninvasive respiratory approach is much more desirable.²²

According to the available data, HFNC may be seen as a further step after COT aiming at preventing mechanical ventilation in the escalating and de-escalating support strategy that could be used as prevention/alternative/integration of NIV (Figure 2).²³

Despite the favorable peculiarities of HFNC that are likely to expand its field of applications in a larger population of ARF patients, some drawbacks have to be highlighted: i) setting (flow, temperature, FiO₂) of the device and choice of the correct size of the nasal cannula should be carefully tailored to each case; ii) environment should be chosen with caution depending on the likelihood of HFNC failure in patients with-

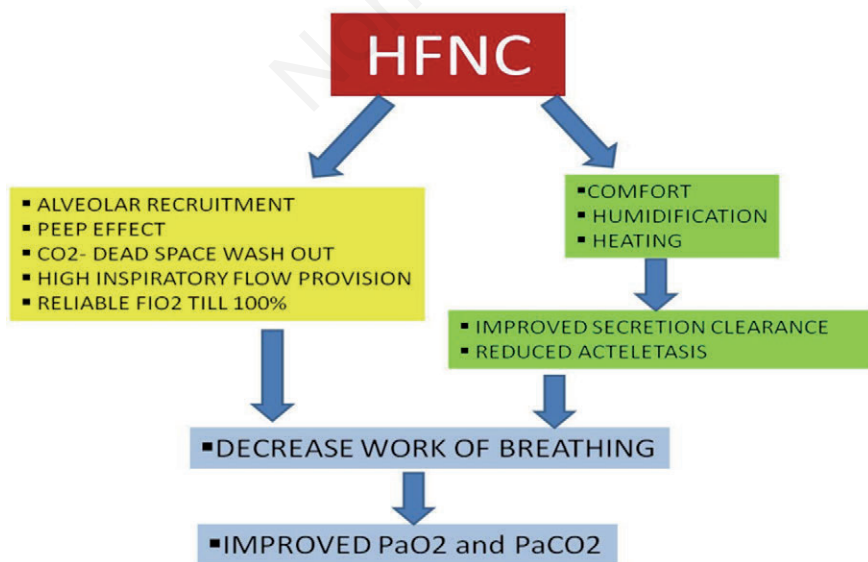


Figure 1. Physiologic effects of HFNC.

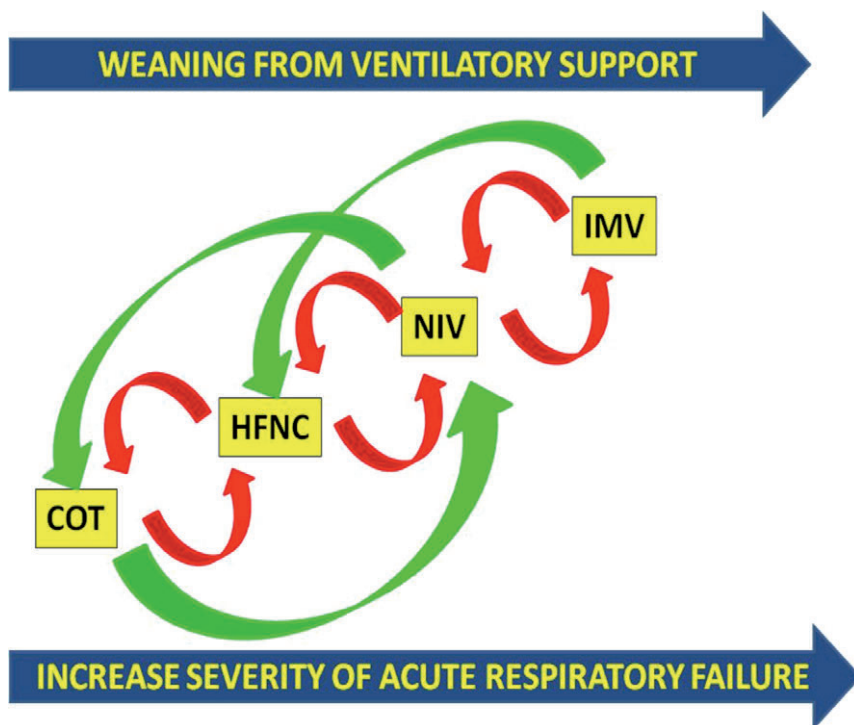


Figure 2. Escalating and de-escalating support in acute respiratory failure. COT, conventional oxygen therapy; HFNC, high-flow nasal oxygen cannula; NIV, non-invasive mechanical ventilation; IMV, invasive mechanical ventilation.

out preset limitations of care (*i.e.* non DNI population) in order to avoid a dangerous delay in providing an escalating ventilator support. Monitoring of patient's conditions and a plan of what to do in case of failure is necessary. A delayed intubation after HFNC failure, like occurs with NIV, has been proved to negatively impact on hospital mortality.^{9,11}

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