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Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: A prospective observational study☆,☆☆

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Abstract

Purpose: The purpose of this study was to determine the impact of high-flow nasal cannula oxygen (HFNC) on patients with acute respiratory failure (ARF) in comparison with conventional oxygen therapy.

Materials and Methods: This was a prospective observational study. Patients with persistent ARF despite oxygen with conventional facemask without indication for immediate intubation were treated with HFNC oxygen. Clinical respiratory parameters and arterial blood gases were compared under conventional and HFNC oxygen therapy.

Results: Twenty patients, aged 59 years (38-75 years) and SAPS2 (simplified acute physiology score) 33 (26.5-38), were included in the study. Etiology of ARF was mainly pneumonia (n = 11), sepsis (n = 3), and miscellaneous (n = 6). Use of HFNC enabled a significant reduction of respiratory rate, 28 (26-33) vs 24.5 (23-28.5) breath per minute (P = .006), and a significant increase in oxygen saturation, oxygen saturation as measured by pulse oximetry 93.5% (90-98.5) vs 98.5% (95.5-100) (P = .0003). Use of HFNC significantly increased Pa_{O_2} from 8.73 (7.13-11.13) to 15.27 (9.66-25.6) kPa (P = .001) and moderately increased Pa_{CO_2}, 5.26 (4.33-5.66) to 5.73 (4.8-6.2) kPa (P = .005) without affecting pH. Median duration of HFNC was 26.5 (17-121) hours. Six patients were secondarily intubated, and 3 died in the intensive care unit.

Conclusion: Use of HFNC in patients with persistent ARF was associated with significant and sustained improvement of both clinical and biologic parameters.

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1. Introduction

Oxygen supply constitutes the first-line therapy of patients with acute respiratory failure (ARF) [1]. It is generally provided via a facemask, nasal cannula, or nasals prongs. Oxygen flow through these devices is limited and generally no greater than 15 L/min. A certain degree of oxygen dilution (delivered oxygen is diluted with room air) may thus occur because of the difference between oxygen flow delivered by the device and patient's inspiratory flow [1], and for this reason, the greater the inspiratory flow, the greater the dilution. If this phenomenon may not impact too much on patients with mild hypoxemia, the situation may be different in more severe patients with more pronounced respiratory failure, bearing in mind that patient inspiratory flow rates may vary between 30 and more than 120 L/min during respiratory failure [2]. New devices now available deliver up to 60 L/min oxygen flow through wide bore nasal cannula. Given the high gas flows delivered by these devices, they are designed to heat and humidify the inspired gas; hence, the generic name of high-flow nasal cannula oxygen therapy (HFNC). If these devices are increasingly used with success in neonates [3-5], their beneficial effects in adults with respiratory failure are yet scarcely reported. A 30-minute evaluation showed an improvement in respiratory parameters in comparison with oxygen delivered via a facemask in intensive care unit (ICU) patients [6], and HFNC has been found to generate a certain level of positive pressure in healthy volunteers and in patients recovering from cardiac surgery. There are no data on a longer evaluation in the ICU. We, thus, aimed to investigate the effect of HFNC to alleviate respiratory distress and ameliorate oxygenation in adult ICU patients with ARF.

2. Methods

A prospective, observational study was conducted in a university hospital 12-bed ICU to investigate the effects of HFNC of respiratory parameters of patients with ARF. The Ethics Committee of the French Society of Intensive Care Medicine (SRLF) approved the study and did not require informed consent because use of HFNC is part of our common practice in these patients. All procedures were routine. Patients and/or family were, however, informed of the study, its purpose, and objectives.

2.1. Study population

Patients who were admitted to the ICU for persistent ARF (defined as oxygen saturation as measured by pulse oximetry <96% and/or a respiratory ≥25 beats per minute while receiving oxygen through a facemask at an estimated fraction of inspired oxygen [Fio_2] >50%) were eligible for inclusion in the study. Patients were excluded if they required immediate intubation.

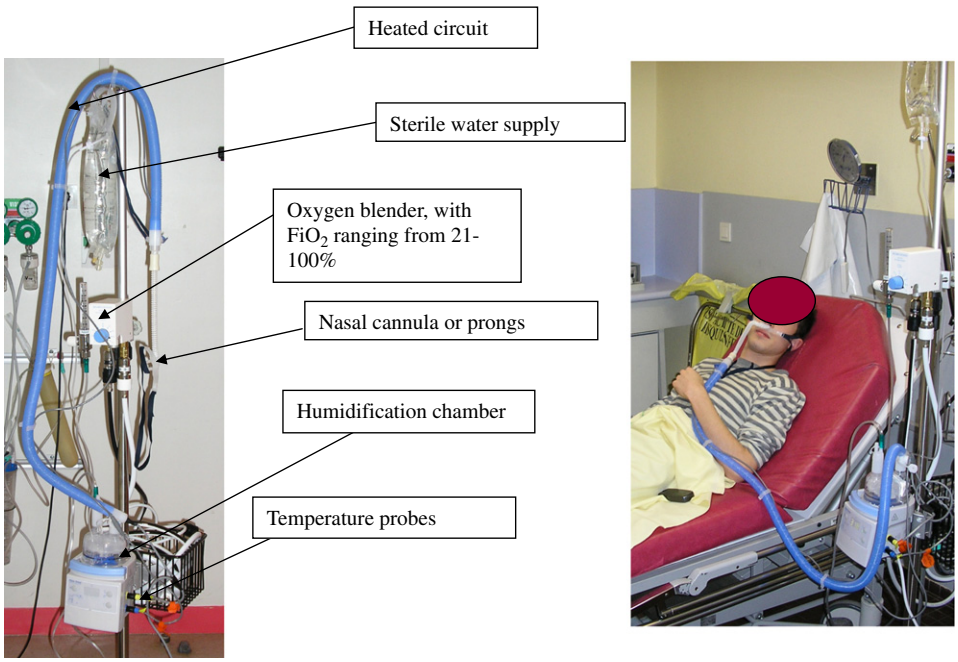

Fig. 1 Shows the device of HFNC. Air and oxygen are mixed through a blender to achieve the desired Fio_2 and flow. The gas mixture is admitted to the humidification chamber where it is heated and humidified. It is then delivered to the patient via a heated circuit to avoid heat loss and condensation and finally via wide bore nasal prongs or cannula.

2.2. Study design

Conventional oxygen was given through a high-Fio_2, nonrebreathing facemask (Hudson RCI; Teleflex medical, High Wycombe, UK). High-flow nasal cannula oxygen therapy was delivered via a dedicated high-flow delivery system (Optiflow; Fisher&Paykel, Auckland, New Zealand) (Fig. 1). Oxygen flows were set by the attending physician based on the patient's condition.

2.3. Data handling

Patient characteristics were collected along with etiology of ARF and need and indication for subsequent intubation and mechanical ventilation. Respiratory parameters were continuously monitored. Arterial blood gases were obtained during conventional oxygenation and the earliest possible after HFNC initiation, at the attending physician's discretion.

2.4. Statistical analysis

The estimated sample size to detect a difference of 4% in oxygen saturation before and after HFNC was 19 patients to achieve a statistical power of 80%. Results are expressed as median (25-75 percentiles). Results obtained before and after HFNC were compared with the Wilcoxon nonparametric test. Friedman test for repeated measurements was used to compare changes over time. Dunn multiple comparison test was used if overall P value was significant. Categorical variables were compared by χ^2 test. A difference was considered significant when $P < .05$.

3. Results

Twenty patients were included in the study. Their baseline characteristics are detailed in Table 1. Ten were male, and the median age was 59 years (38-75 years). Their SAPS2 score was 33 (26.5-38), yielding a 16% risk of hospital mortality. Etiology of ARF was mainly community-acquired pneumonia (n = 11), sepsis (n = 3), and miscellaneous (n = 6). Median duration of ARF before inclusion was short, 2.25 (0.75-10) hours. Median oxygen flow was significantly greater during HFNC than during facemask therapy, 40 L/min (32.5-50.0) vs 15 L/min (9-15)

Table 1 Patient characteristics

Patient characteristics		N = 20
Sex ratio (M/F)		10/10
Age (y)		59 (38-75)
SAPS2		33 (26.5-38)
Patient origin	Emergency department	14
	Prehospital setting	4
	Medical ward	2
Comorbidity	COPD	1
	Lung cancer	2
	Bronchiectasis	1
	Asthma	1
	HIV infection	1
	Active smoking	3
	History of pneumonia	4
Indications	Community-acquired pneumonia	11
	Pulmonary embolism	1
	COPD exacerbation	1
	TRALI	1
	Purulent pleural effusion	1
	Pulmonary contusion	1
	Cardiogenic pulmonary edema	1
	Postextubation ARF	1
	Other [a]	2
Hospital-acquired pneumonia		1 (after tracheal intubation)
Duration of HFNC therapy (h)		26.5 (17-121)
Hospital stay (d)		8 (4-10)
Outcome	Intubation	6
	Transfer to general ward	14
	Death	3

TRALI indicates transfusion-related acute lung injury; COPD, chronic obstructive pulmonary disease.
[a] One respiratory distress because of lung metastasis and one sepsis-related ARF.

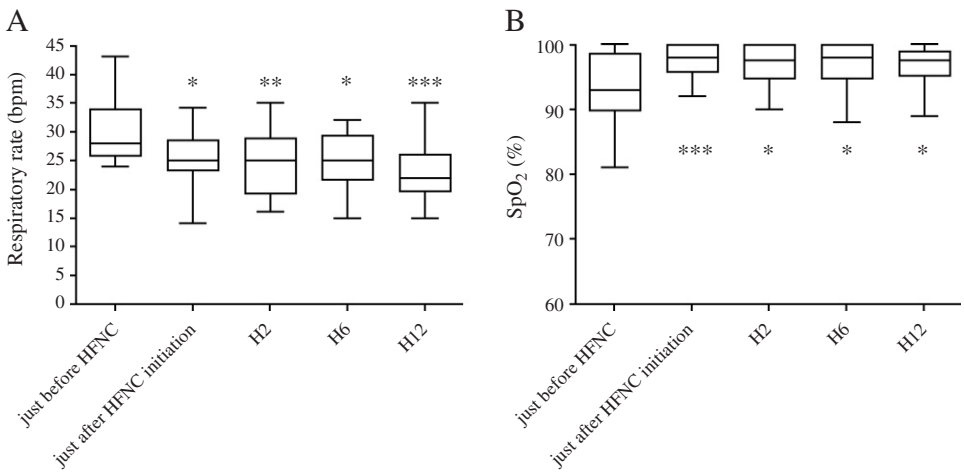

Fig. 2 Shows the evolution of respiratory rate (panel A) and pulse oximetry (pane B) before and after initiation of HFNC. Friedman test for repeated measurements indicated a significant difference in respiratory rate ($P < .0002$) and pulse oximetry ($P = .0009$) overtime. Post test Dunn comparison showed a sustained decrease in respiratory rate and increase in pulse oximetry (*$P < .05$; **$P < .01$; ***$P < .001$).

($P = .0003$), respectively. Estimated delivered Fio_2 were similar. Use of HFNC enabled a significant reduction of respiratory rate, 28 (26-33) vs 24.5 (23-28.5) breath per minute ($P = .006$), and a significant increase in oxygen saturation, oxygen saturation as measured by pulse oximetry 93.5% (90-98.5) vs 98.5% (95.5-100) ($P = .0003$). There was a nonsignificant trend toward decreased heart rate under HFNC: 105 (92-116) vs 100 (87-110) cycles per minute ($P = .11$). The median delay between HFNC initiation and arterial blood gas was 2 (1-4.5) hours. Use of HFNC significantly increased Pao_2 from 8.73 (7.13-11.13) to 15.27 (9.66-25.6) kPa ($P = .001$); did not affect pH, 7.44 (7.38-7.48) vs 7.43 (7.39-7.45) ($P = .44$); and moderately increased $Paco_2$, from 5.26 (4.33-5.66) to 5.73 (4.8-6.2) kPa ($P = .005$). Improvement in Pao_2 remained significant when keeping only those patients for whom the delay between onset of HFNC and arterial blood gas did not exceed 3 hours (n = 13) (data not shown). Median duration of HFNC was 26.5 (17-121) hours. The maximum duration was 156 hours, and 6 patients had more than 100 hours of continuous use. Six patients were secondarily intubated after a median delay of 17.5 hours (1.5-59.0) after HFNC initiation. Reasons for intubation were septic shock, gastrointestinal hemorrhage, and the 4 others because of pneumonia progression with deterioration of their respiratory status. Apart from these patients, benefit of this technique was sustained in the other patients as depicted in Fig. 2 that shows significant differences in respiratory parameters between baseline and different time points after HFNC initiation. All but one (for whom a do-not-resuscitate decision was taken) of these patients were discharged alive from the ICU after having been successfully weaned from HFNC with progressive decrease in Fio_2 and flow rate. Two of the intubated patients died under mechanical ventilation. The last one was successfully weaned and discharged alive.

4. Discussion

This study shows for the first time the beneficial effects of HFNC as first-line treatment for ICU patients with ARF. Its main results can be summarized as follows: (1) all respiratory parameters were improved after 1 hour of HFNC; (2) use of HFNC leads to a significant improvement in oxygenation; (3) HFNC was well tolerated for long periods with sustained benefits in patients who were not intubated. These results obtained in the "real life" of the management of ARF indicate that patients can be safely managed during several days with HFNC. This technique offers an effective alternative to conventional oxygenation. Our results constitute the prerequisite for a randomized study comparing conventional oxygen therapy and HFNC.

As stated earlier, there is very limited published experience with HFNC in adults with ARF. Roca et al [6] were the first to present promising data on respiratory and oxygenation parameters in ICU patients. They showed significant improvement in both clinical and biologic parameters after 30 minutes of HFNC in comparison with standard facemask oxygen therapy. Of note, the median duration of conventional treatment before HFNC initiation was more than 4 days, which precludes from any conclusion on the effect of HFNC in the immediate management of ARF. In addition, HFNC was used for 30 minutes only, providing no data on the long-term effects of this device. To the best of our knowledge, no other data are available in the same context.

Several factors can account for the observed improvement in respiratory parameters. The high oxygen flows delivered by HFNC may substantially correct hypoxemia by several mechanisms and, thus, contribute to the alleviation of respiratory distress symptoms. First, the blender that equips the device generates much greater flows that result in an important reduction in oxygen dilution by establishing a better matching between the patient's inspiratory flow

demand and the delivered gas flow. This also counteracts the resistance on inspiratory efforts induced by the nasopharyngeal's distensibility [7]. Second, a positive airway pressure effect, also generated by the high flow, provides a certain level of pulmonary distending pressure and alveolar recruitment. This effect has been documented in healthy volunteers [8] and patients recovering from cardiac surgery [9]. In this study, investigators found that HFNC with 35 L/min flow generated mean nasopharyngeal pressure ranging from 1.54 to 5.34 cm H_2O [8]. One can legitimately imagine that these pressures may be even greater with increasing levels of flow. Third, the high flows enhance a washout of the nasopharyngeal dead space, thus contributing to an improved fraction of alveolar gases [10]. Finally, increased patient comfort may also contribute to the beneficial results obtained with HFNC. This has been reported with HFNC (with a decrease in mouth dryness) in comparison with conventional oxygen therapy. Although the comfort parameter was not systematically monitored in our study, interruption of HFNC because of discomfort was never reported. Our very first patient managed with HFNC had severe transfusion-related acute lung injury that required noninvasive ventilation because of the severity of respiratory failure. High-flow nasal cannula oxygen therapy was tried because the patient did not tolerate noninvasive ventilation. High-flow nasal cannula oxygen therapy was pursued thereafter until full recovery.

This study has obvious limitations. First of all, it was not a randomized controlled study. However, it seemed difficult (and unethical?) to undergo a randomized controlled trial with a technique for which—at that time—no data in adults requiring ICU admission for ARF were available. Second, the observational design of the study and the relatively loose criteria to define persistent respiratory failure led to considerable disparity in Pa_{O_2} levels before HFNC initiation. Hence, improvement in Pa_{O_2} may have been greater in a more selected and homogenous population. We were, however, interested in providing real-life data. Third, as in the study of Roca et al [6], actual delivered Fi_{O_2} was not measured in our study. We solely relied on the manufacturers' specifications. Part of the improvement in oxygenation observed with HFNC might have been related to the delivery of higher Fi_{O_2} in comparison with high-flow facemasks. True delivered Fi_{O_2} with these masks varies considerably and depends also on patient minute ventilation. However, given the characteristics of our facemask (use of a reservoir) and the oxygen flow rates used, we believe that most of the patients if not all of them had similar Fi_{O_2} than during HFNC. We, thus, believe that the other factors mentioned above also contributed to the significant improvement observed with HFNC, even if their exact contribution is not known.

Pneumonia was the main cause of respiratory failure in our patients, and we believe that patients with hypoxemic lung infection are good candidates for initial management with HFNC. Because patients were not randomized, one can only speculate on how many were not intubated, thanks to HFNC. However, secondary intubation was required in 6 patients yielding a 30% HFNC "failure" rate; a figure that compares fairly with noninvasive ventilation [11]. Of note, ICU-acquired pneumonia was not diagnosed in our patients during HFNC, even in those with the longest duration. The only episode that occurred was diagnosed after several days of mechanical ventilation in a patient who required intubation. Obviously, a randomized controlled trial will have to demonstrate the possible reduction in intubation rate in patients treated with HFNC (and the potential for a subsequent decrease in ventilator-acquired pneumonia), but our results along with others [6] now provide encouraging data to launch such a trial. The question that arises concerns the comparators for this trial: should HFNC be compared solely to conventional oxygen therapy, or should noninvasive ventilation also be included? Our bias is that HFNC's place in the supportive management of hypoxemic ARF is in between conventional oxygen therapy and noninvasive ventilation. Thus, it may seem reasonable to compare these 3 techniques.

Taken together, our results indicate that HFNC improves respiratory parameters and oxygenation in patients with ARF. This technique was well tolerated for several days (a finding in agreement with a recent report [12]) probably avoiding invasive mechanical ventilation and its potential drawbacks in some of them.

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