High-Flow Oxygen Therapy in Acute Respiratory Failure

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OBJECTIVE: To compare the comfort of oxygen therapy via high-flow nasal cannula (HFNC) versus via conventional face mask in patients with acute respiratory failure. Acute respiratory failure was defined as blood oxygen saturation < 96% while receiving a fraction of inspired oxygen ≥ 0.50 via face mask. METHODS: Oxygen was first humidified with a bubble humidifier and delivered via face mask for 30 min, and then via HFNC with heated humidifier for another 30 min. At the end of each 30-min period we asked the patient to evaluate dyspnea, mouth dryness, and overall comfort, on a visual analog scale of 0 (lowest) to 10 (highest). The results are expressed as median and interquartile range values. RESULTS: We included 20 patients, with a median age of 57 (40–70) years. The total gas flow administered was higher with the HFNC than with the face mask (30 [21.3–38.7] L/min vs 15 [12–20] L/min, *P* < .001). The HFNC was associated with less dyspnea (3.8 [1.3–5.8] vs 6.8 [4.1–7.9], *P* = .001) and mouth dryness (5 [2.3–7] vs 9.5 [8–10], *P* < .001), and was more comfortable (9 [8–10]) versus 5 [2.3–6.8], *P* < .001). HFNC was associated with higher P_{aO_2} (127 [83–191] mm Hg vs 77 [64–88] mm Hg, *P* = .002) and lower respiratory rate (21 [18–27] breaths/min vs 28 [25–32] breaths/min, *P* < .001), but no difference in P_{aCO_2}. CONCLUSIONS: HFNC was better tolerated and more comfortable than face mask. HFNC was associated with better oxygenation and lower respiratory rate. HFNC could have an important role in the treatment of patients with acute respiratory failure. *Key words: acute respiratory failure; respiratory insufficiency; treatment; oxygen therapy; high-flow nasal cannula.* [Respir Care 2010;55(4):408–413. © 2010 Daedalus Enterprises]

Introduction

Administration of oxygen is an essential support measure to maintain proper tissue oxygenation in patients with acute respiratory failure (ARF). The conventional oxygen delivery methods have been nasal prongs, nose mask, and face mask, but the oxygen provided by the conventional systems may not suffice in patients with ARF.

High-flow oxygen (up to 50 L/min) via nasal cannula, combined with a heated humidification system, may have several advantages. High-flow nasal cannula (HFNC) can decrease oxygen dilution,[1-3] reduce respiratory dead space,[2] and generate some positive airway pressure, because of the expiratory resistance generated by the continuous high flow delivered.[2,3] The heated humidification can facilitate secretion clearance and decrease the development of bronchial hyper-response symptoms.[4] HFNC has been evaluated in healthy subjects,[3] patients with stable chronic obstructive pulmonary disease,[2] and in patients after abdominal surgery.[1] To our knowledge, the experience with HFNC in patients with ARF is limited to sporadic cases.[5,6]

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Dr Roca and Dr Masclans have disclosed relationships with Fisher & Paykel Healthcare. Dr Riera and Dr Torres have disclosed no conflicts of interest.

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Thus, the primary aim of this study was to compare the subjective comfort perceived by ARF patients receiving oxygen via face mask versus via HFNC, as measured with a visual analog scale. We previously reported this study in an abstract.[7]

Methods

The manufacturer of the HFNC system we used did not provide any form of support or consultation in the design, conduct, or writing of this study.

Study Population

We included 20 patients with ARF, defined as a blood oxygen saturation (measured via pulse oximetry [S_{pO_2}]) $< 96\%$ while receiving humidified oxygen via face mask, with a fraction of delivered oxygen (F_{DO_2}) of ≥ 0.5. The exclusion criteria were: unstable clinical status (eg, marked changes in respiratory variables in the 60 min prior to inclusion in the study); need for endotracheal intubation; decreased consciousness (Glasgow coma scale < 14); severe hemodynamic instability despite fluid therapy and vasopressors; severe failure of > 2 organs apart from respiratory failure; pregnancy; and lack of patient cooperation.

The study was approved by the ethics committee of our center, and patients gave their informed consent to participate.

Study Design

This was a prospective, comparative study of sequential interventions. The patients were resting in bed in partial sitting position, and we recorded baseline respiratory variables. The oxygen was humidified with a bubble humidifier (Respiflo Water and MN Adapter, Tyco Healthcare, Gosport, United Kingdom) and administered via standard face mask (Oxinova, Carburos Medica, Spain) for 30 min, during which the patient was allowed to use a combination of face mask and conventional nasal cannula to increase the total oxygen flow, in which case the total flow delivered was the sum of the flow from the face mask and cannula.

We then delivered the oxygen via HFNC (Optiflow, Fisher & Paykel, Auckland, New Zealand) (Fig. 1) at an initial flow of 20–30 L/min, with an F_{DO_2} identical to that with the face mask. The total flow was increased in each patient according to the criteria of the attending physician. The same F_{DO_2} was maintained over the entire testing period.

For both face mask and HFNC, F_{DO_2} was estimated following the manufacturer's specifications.

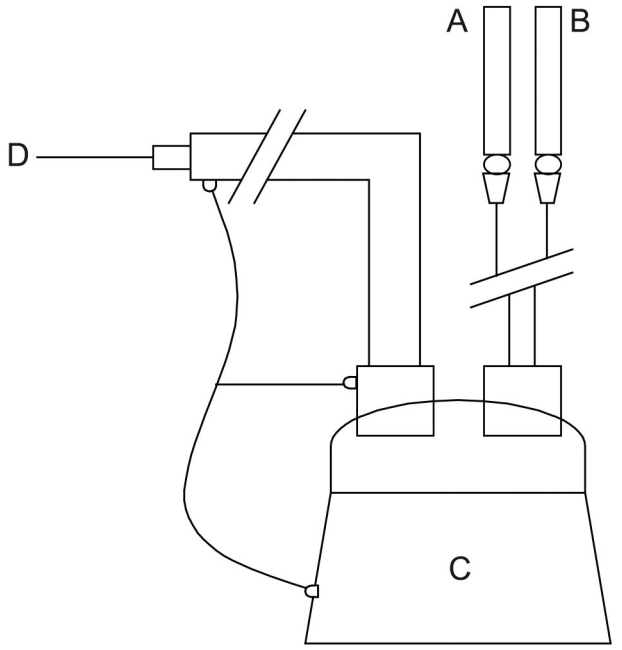

Fig. 1. Diagram of the high-flow nasal cannula. A: Compressed air source. B: Oxygen source. C: Heated humidifier. D: Nasal cannula.

At the end of each 30-min period we asked the patient for his or her subjective assessment of the device (see below) and took a sample of arterial blood. Following the two 30-min study periods we asked the patient which of the oxygen systems he or she wanted to continue using.

Variables Measured

We recorded the Sequential Organ Failure Assessment[8] at the time of enrollment, and the Acute Physiology and Chronic Health Evaluation score[9] at intensive care unit (ICU) admission. We defined multiple-organ dysfunction syndrome as failure of > 2 organs. We estimated the degree of radiologic involvement as the number of affected quadrants on the chest radiograph.[10] Throughout the study periods we monitored electrocardiography variables, blood pressure, respiratory variables, and adverse events related to the use of the oxygen therapy systems.

We asked each patient to subjectively evaluate the 2 oxygen therapy methods, after 30 min of use in stable conditions. With a visual analog scale that ranged from 0 (lowest) to 10 (highest), we asked the patient to rate his or her dyspnea, mouth dryness, and overall comfort.[11]

We also measured arterial blood gas values, acid-base balance, respiratory rate, and S_{pO_2}.

Statistical Analysis

The estimated sample size was 20 patients to achieve a statistical power of 80% for detecting that an observation

Table 1. Baseline Characteristics

Patients (*n*)	20
Age (median and IQR y)	57 (40–70)
Male (*n*, %)	14 (70)
APACHE II score (median and IQR)	14.0 (10.5–17.5)
SOFA score (median and IQR)	4.0 (3.2–6.0)
Multiple organ dysfunction syndrome (*n*, %)	4 (20)
Intrapulmonary ARF (*n*, %)	17 (85)
Extrapulmonary ARF (*n*, %)	3 (15)
Etiology of ARF (*n*, %)	
Pneumonia	13 (65)
Extrapulmonary ALI	3 (15)
Acute lung-graft rejection	1 (5)
Severe asthma exacerbation	1 (5)
COPD exacerbation	1 (5)
Cardiogenic lung edema	1 (5)
Duration of ARF before inclusion (median and IQR)	4 (3–8)
Number of affected quadrants on chest radiograph (median and IQR)	3 (2–4)

APACHE II = Acute Physiology and Chronic Health Evaluation II
SOFA = Sequential Organ Failure Assessment
ARF = acute respiratory failure
ALI = acute lung injury
COPD = chronic obstructive pulmonary disease

in one group was lower than in the other, at a probability of 0.756, with the Mann-Whitney non-parametric test for independent data, with a protection against type 1 error of 5% bilaterally. Since the study design is actually for dependent data, it was expected that the statistical power would be higher, according to the correlation found.[12]

The results are expressed as the median and interquartile range values, or frequencies (percentage). We compared the results with the Wilcoxon non-parametric test. The analyses were conducted with statistics software (SPSS version 13.0, SPSS, Chicago, Illinois). Significance was set at a 2-tailed *P* value of .05.

Results

General Characteristics

Twenty patients were included. Fourteen (70%) were men. The median age was 57 (40–70) years. Table 1 shows the cohort's baseline characteristics. Nineteen patients (95%) were admitted to the ICU due to hypoxemic ARF. The median duration of ARF before inclusion in the study was 4 (3–8) days.

Subjective Assessment and Respiratory Variables

The results of the subjective assessment show a significant improvement in the 3 variables analyzed with the use of HFNC (Table 2). In the evaluation of respiratory variables, there were no significant differences between the baseline values and those at the end of 30 min of face mask use. However, with HFNC there was a significant increase in P_{aO_2} and a reduction in respiratory rate (Fig. 2), without hypercapnia or acidosis. Arterial blood samples were not obtained from the 4 patients who did not have arterial catheters. There was no significant change in mean arterial pressure or heart rate. Once the testing period had been completed and the patients were asked to choose which of the 2 oxygen therapy systems they wanted to continue using, all chose the HFNC.

Adverse Effects

Five patients (25%) reported some mild adverse effects that may have been related to the HFNC. The most common (3 patients) was a sensation of cervical-thoracic discomfort that appeared during the initial period of increasing flow, and immediately disappeared when flow was decreased. Another patient said that the gas temperature was too high. In all the latter cases the effects appeared in the initial few minutes of the testing period and had completely disappeared by the end of the testing period. The other patient who reported an adverse effect had nonspecific nasal discomfort, and nasal mucosal lesions were detected during HFNC use. On the other hand, mucosal lesions were seen before HFNC in another patient, probably related to the previous use of conventional nasal cannula.

Discussion

This study presents the first results of applying humidified HFNC in patients with ARF. HFNC was associated with less dyspnea and mouth dryness, and greater overall comfort.

The dyspnea decrease may be due to several factors. With HFNC the higher flow delivered, the correction of hypoxemia, and the reduction in the respiratory rate may play an important role. Second, although there was significantly less mouth dryness, this variable was likely to have continued improving after the 30 min of the study, because 30 min may have been too short to determine the true effects of the heated humidification system on mouth dryness. Third, the patients found HFNC significantly more comfortable, and there may be several reasons for this. The above-mentioned benefits surely played a part. Underhumidified oxygen therapy is also associated with discomfort in critically ill patients.[13] That HFNC does not affect speaking and allows food ingestion could also play a role. This increased comfort is consistent with the fact that all the patients chose to continue with HFNC after having tried it.

Table 2. Subjective Evaluation and Respiratory, Hemodynamic, and Gas-Exchange Data*

	Face Mask	HFNC	*P*
Subjective Evaluation			
Dyspnea	6.8 (4.1–7.9)	3.8 (1.3–5.8)	.001
Mouth dryness	9.5 (8.0–10.0)	5 (2.3–7.0)	< .001
Overall comfort	5.0 (2.3–6.8)	9.0 (8.0–10.0)	< .001
Respiratory and Gas-Exchange Variables			
Total oxygen flow (L/min)	15.0 (12.0–20.0)	30.0 (21.3–38.7)	< .001
Fraction of delivered oxygen	1.0 (0.8–1.0)	1.0 (0.8–1.0)	.32
Respiratory rate (breaths/min)	28 (25–32)	21 (18–27)	< .001
pH†	7.42 ± 7.38–7.47	7.44 (7.38–7.50)	.06
P_{aO_2} (mm Hg)†	77 (64–88)	127 (83–191)	.002
P_{aCO_2} (mm Hg)†	37 (33–45)	37 (32–43)	.51
HCO_3^- (mmol/L)†	25.0 (22.1–28.5)	24.5 (22.2–29.1)	.09
Base excess (mmol/L)†	1.0 (−2.3–4.8)	–1.0 (–2.3 to 5.3)	.055
S_{pO_2} (%)	95 (91–97)	98 (96–99)	.002
Hemodynamic Variables			
Mean arterial pressure (mm Hg)	87 (76–94)	86 (71–93)	.36
Heart rate (beats/min)	94 (77–112)	85 (73–108)	> .99

* All values are median and interquartile range.
† Only in patients with an arterial catheter.
HFNC = high-flow nasal cannula
S_{pO_2} = blood oxygen saturation measured via pulse oximetry

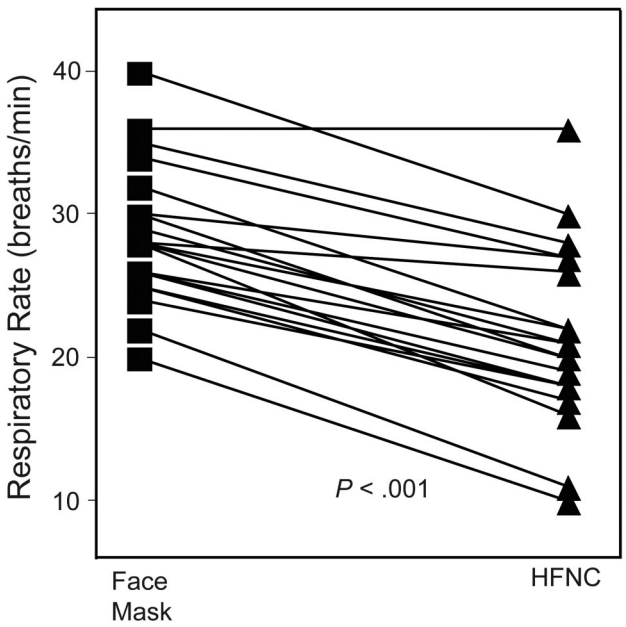

Fig. 2. Change in respiratory rate with change from face mask to high-flow nasal cannula (HFNC).

We assessed the variables studied with visual analog scales. These scales are solid, well recognized systems for measuring patients' perceptions of variables such as dyspnea.[14-18] In fact, the visual analog scale is considered the most appropriate instrument for repeated measurement of a subjective variable in a given patient, as it is sufficiently sensitive to detect changes occurring minute by minute.[19]

The effect of HFNC on oxygenation is equally important. As compared to the conventional oxygen mask, we found improvement in oxygenation after 30 min of HFNC. We did not measure fraction of inspired oxygen (F_{IO_2}) because that would have required placing a pharyngeal catheter, which might have generated artifacts in the subjective evaluations. However, the oxygenation improvement with HFNC might have been due to a higher F_{IO_2} achieved with the higher flow with HFNC. At low flow the oxygen is diluted with ambient air because the oxygen flow is lower than the patient's inspiratory flow demand. Wettstein et al[20] measured the F_{IO_2} in the pharynx during nasal cannula at low flow (1–6 L/min) and high flow (6–15 L/min). There was a progressive increase in pharyngeal F_{IO_2} with each increase of oxygen flow. That study analyzed only flows up to 15 L/min, but the present study shows how this effect may persist and possibly increase with higher flow in patients with ARF.

Nevertheless, with a given F_{IO_2}, other factors may contribute to improved oxygenation with HFNC. First, continuous high flow can wash-out exhaled air from the upper airway and thus reduce dead space.[2] Second, nasal cannula seems to be better tolerated than face mask, which has been reported to improve patient adherence to therapy and oxygenation.[21] Third, the high flow exerts a continuous positive airway pressure in both healthy

volunteers and patients with chronic obstructive pulmonary disease,[3] who additionally showed an increase in exercise capacity. The airway pressure generated is directly related to the flow administered; tracheal pressure of up to 5 cm H_2O has been recorded with a flow of 50 L/min.[3] In the present study, however, airway pressure was not measured. Moreover, the reported effect was observed with higher flows than we used in the majority of patients in this study. Thus, it is unlikely that a continuous positive airway pressure effect would have contributed to improved oxygenation in our patients.

Also, the heated humidifier system may indirectly affect oxygenation. Active humidification improves mucociliary function, facilitates secretion clearance, and decreases atelectasis formation, which improves ventilation-perfusion ratio and oxygenation. However, in the present study it is unlikely that those factors could have affected oxygenation after only 30 min. On the other hand, heated humidification systems may attenuate the development of bronchial hyper-response symptoms,[4] so humidified HFNC may be particularly beneficial in patients with respiratory infection, chronic obstructive pulmonary disease, or bronchial asthma.

The pronounced reduction in respiratory rate in the present study is also important, particularly because it was not associated with changes in the P_{aCO_2} or pH. This finding is consistent with other reported data[1,2] and may have contributed to the improvement in dyspnea and comfort.

There were some adverse effects with HFNC, but several points should be taken into account when interpreting these results. First, all the adverse effects from HFNC were mild. Second, the sensation of cervical-thoracic discomfort disappeared when the flow was decreased. In addition, outside the testing period we found that higher flows could be achieved with HFNC with no cervical-thoracic discomfort. Similarly, the feeling of excessive gas temperature, reported by one patient, also disappeared during the testing period. Third, some of the patients received oxygen at the beginning of the study with a combination of face mask and conventional nasal cannula. Therefore, the nasal mucosal lesion discovered during HFNC could have been the result of an additive effect of both systems, as suggested by the fact that such a lesion was observed in one patient before HFNC. Therefore, we believe that HFNC could be considered comfortable, especially given that after the testing period all the patients chose to continue with HFNC.

Limitations

First, we did not use a randomized design; instead, patients were allowed to choose which of the 2 oxygen therapy systems they wanted to continue with. Second, we could not quantify the relative contribution of each factor involved in the HFNC system (nasal cannula, high flow, warm gas, humidification) to the results obtained. Third, in an attempt to avoid generating artifacts in the subjective evaluation, we did not measure the F_{IO_2}. Fourth, the patients could not be blinded to the systems being tested. Nevertheless, these limitations do not detract from the favorable results obtained with HFNC in patients with ARF in a study whose main objective was to compare the comfort of the 2 oxygen systems.

Conclusions

HFNC can improve the clinical tolerance of oxygen therapy in patients with ARF. In addition to the subjective benefit, our patients showed improved oxygenation and a reduced respiratory rate. Thus, we consider this HFNC system useful for integrated treatment of ARF, although further investigation is needed to determine the clinical scenarios in which its benefits will have the greatest impact.

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