Heated and Humidified High-Flow Oxygen Therapy Reduces Discomfort During Hypoxemic Respiratory Failure

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BACKGROUND: Non-intubated critically ill patients are often treated by high-flow oxygen for acute respiratory failure. There is no current recommendation for humidification of oxygen devices. METHODS: We conducted a prospective randomized trial with a final crossover period to compare nasal airway caliber and respiratory comfort in patients with acute hypoxemic respiratory failure receiving either standard oxygen therapy with no humidification or heated and humidified high-flow oxygen therapy ($HHFO_2$) in a medical ICU. Nasal airway caliber was measured using acoustic rhinometry at baseline, after 4 and 24 hours (H4 and H24), and 4 hours after crossover (H28). Dryness of the nose, mouth, and throat was auto-evaluated and assessed blindly by an otorhinolaryngologist. After the crossover, the subjects were asked which system they preferred. RESULTS: Thirty subjects completed the protocol and were analyzed. Baseline median oxygen flow was 9 and 12 L/min in the standard and $HHFO_2$ groups, respectively ($P = .21$). Acoustic rhinometry measurements showed no difference between the 2 systems. The dryness score was significantly lower in the $HHFO_2$ group at H4 (2 vs 6, $P = .007$) and H24 (0 vs 8, $P = .004$). During the crossover period, dryness increased promptly after switching to standard oxygen and decreased after switching to $HHFO_2$ ($P = .008$). Sixteen subjects (53%) preferred $HHFO_2$ ($P = .01$), especially those who required the highest flow of oxygen at admission ($P = .05$). CONCLUSIONS: Upper airway caliber was not significantly modified by $HHFO_2$, compared to standard oxygen therapy, but $HHFO_2$ significantly reduced discomfort in critically ill patients with respiratory failure. The system is usually preferred over standard oxygen therapy. *Key words: respiratory failure; high-flow oxygen therapy; upper airway caliber; upper airway dryness; humidification; pain.* [Respir Care 2012;57(10):1571–1577. © 2012 Daedalus Enterprises]

Introduction

Supplemental oxygen is among the first-line treatments for acute respiratory failure. No recommendations exist concerning oxygen heating, humidification, or delivery techniques in spontaneously breathing patients.[1] Breathing a high flow of dry, cold oxygen can cause dryness of the upper airway mucosa, which leads to discomfort and pain.[2]

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The use of dry gases during nasal CPAP in healthy individuals has been shown to induce a large increase in nasal resistance.[3] Inadequate humidification may also increase the risk of intubation difficulties after failure of noninvasive ventilation.[4] On the other hand, warming and humidification have been shown to improve lung mucociliary clearance in patients with bronchiectasis.[5]

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Humidification systems, such as heat and moisture exchangers and heated humidifiers, have been studied chiefly during endotracheal mechanical ventilation. Heated humidifiers with adequate regulation systems are considered the most efficient humidification devices for mechanical ventilation.[6] These devices rely on the evaporation of water in the humidification chamber, depending on the heater plate temperature.[7] Optimal conditions for humidification are difficult to define, but delivering inspiratory gas significantly different from physiologic temperature (37°C) and relative humidity (100%) may impair the function of the mucociliary apparatus.[8,9]

Few studies have compared outcomes between humidified and non-humidified oxygen therapy in spontaneously breathing patients. Some studies compared bubble humidifiers with no humidification but were performed in stable patients receiving low-flow oxygen outside the ICU. The difference in symptoms of patient discomfort was small or nonsignificant.[10,11] Chanques et al recently showed that heating and humidification improved the tolerance of oxygen therapy and decreased the symptoms of dryness.[12] The purpose of this study was to compare the effect of standard oxygen therapy without humidification to heated and humidified high-flow oxygen therapy ($HHFO_2$) on nasal airway caliber and a dryness score.

QUICK LOOK

Current knowledge

High-flow oxygen via nasal cannula is often used to treat acute hypoxemic respiratory failure. The required temperature and humidity of the delivered oxygen to maximize patient comfort and prevent airway complications is unknown.

What this paper contributes to our knowledge

Compared to traditional high-flow nasal oxygen, humidified high-flow nasal oxygen improved patient comfort by reducing nasal dryness, but did not improve nasal airway caliber.

Methods

Settings and Subjects

This prospective randomized single-center trial with a final crossover period was conducted in the medical ICU of Hôpital Henri Mondor, Assistance Publique des Hôpitaux de Paris, Paris, France, from December 2009 to December 2010. Consecutive patients were included if they required at least 4 L/min of oxygen to maintain the S_{pO_2} above 95%. Exclusion criteria were the use of noninvasive or invasive mechanical ventilation, and presence of delirium impairing the ability of the subject to rate dryness and preference for one of the 2 oxygen delivery systems.

The local ethics committee (Comité de Protection des Personnes) approved the study design. All subjects gave their written informed consent to study participation prior to study inclusion.

Materials

Standard oxygen was delivered with a flow meter from wall oxygen, without humidification, as currently recommended at our institution. Humidification over cold water is of very limited efficacy, and studies conducted in hospitalized patients (but not in the ICU) concluded that there were no or few difference between use of bubble humidifier and no humidification.[10] After a cost-effectiveness study, our institution decided to stop using the bubble humidifier. Current knowledge does not support that this places the patient at a disadvantage. The oxygen flow was set to maintain S_{pO_2} above 95%. The heated humidifier (Optiflow MR850, Fisher & Paykel Healthcare, Auckland, New Zealand) consisted of a gas-water chamber at 37°C, which delivered 44 mg H_2O/L, through which the oxygen traveled before delivery to the subject. A heated wire along the inspiratory circuit prevented water condensation in the tubes.[6] Flow was set at 4 L/min in all subjects. The F_{iO_2} was set to maintain S_{pO_2} above 95%.

Acoustic rhinometry measurements were done using rhinometrics equipment (RhinoScan SRE2000, Interacoustics, Assens, Denmark). Acoustic rhinometry involves analyzing sound waves reflected from the nasal cavity. By sending a sound pulse into the nose and recording and analyzing the reflected sound, a 2-dimensional picture of the nasal cavity is obtained, from which the volume and cross-sections of the nasal cavity can be deduced. The main benefit of acoustic rhinometry is its capacity to identify the narrowest part of the nasal cavity or minimal cross-sectional area. The measurement is fast and requires only that the patient have a regular breathing pattern for a few seconds (see Supplementary Figure 1 in the supplementary

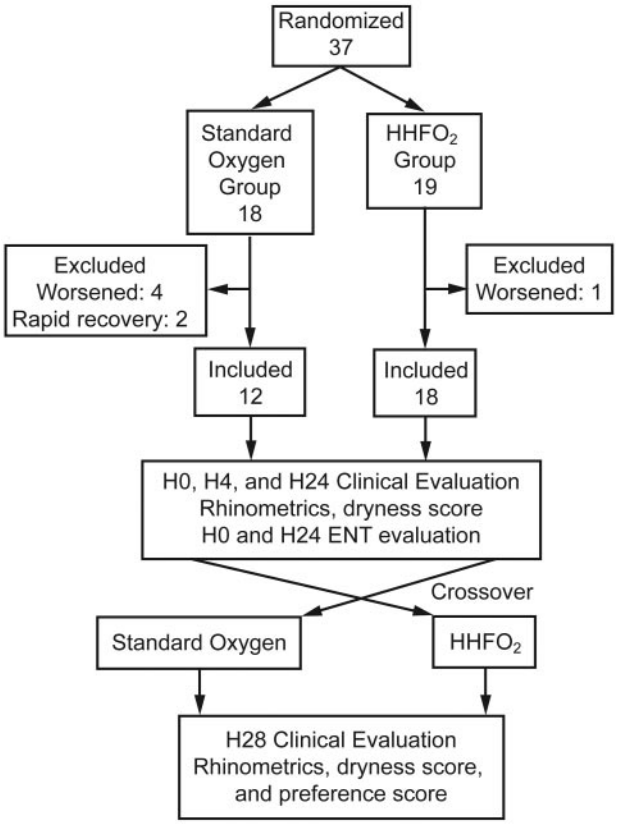

Fig. 1. Study design and flow chart. Inclusion time was hour 0 (H0) and evaluations were done at H4, H24, and H28 after inclusion. The crossover occurred at H24, and subjects switched to the other the device for 4 hours. The rhinometric measurements were acoustic measurements, done by rhinometrics equipment. The dryness numerical scores were evaluated by numerical rating scale. $HHFO_2$ = heated humidified high-flow oxygen therapy. ENT = ear, nose, and throat evaluation.

materials at http://www.rcjournal.com). Acoustic rhinometry is a rapid, objective, painless, noninvasive technique used for assessing nasal airway obstruction.[13]

Direct clinical evaluation by an otorhinolaryngologist was performed at baseline before randomization. The evaluation was repeated after 24 hours by the same specialist, who was blinded to the randomization arm.

Study Design

The subjects were randomized to receive standard oxygen therapy or $HHFO_2$ therapy via a nasal cannula during the first 24 hours, then the crossover occurred and each subject was switched to the other device for 4 hours (Fig. 1). When conducting the feasibility study we noted that most of the subjects decreased their oxygen need below the 4 L/min threshold after 36 hours. Therefore, asking for another 24 hours would have resulted in a large number of drop-outs. This design was done to minimize drop-outs and allowed us to first compare the effects of 24 hours with each device and to assess subject preference for one or the other device after the crossover.

Clinical parameters and rhinometry measurements were collected at baseline (H0), after 4 hours (H4) and 24 hours (H24), and 4 hours after crossover (H28).

Collected Data

We recorded the values for 2 rhinometry variables, on each side: average cross-sectional area between 0–2 cm and 2–4 cm (middle turbinate) from the nares, and the minimal cross-sectional area, thought to correlate with nasal airway resistance.[14]

Discomfort was assessed by evaluating dryness of the nose, mouth, and throat. The subjects used a large-print numerical rating scale adapted for use in the ICU and ranging from 0 (no dryness) to 10 (maximum dryness) (Appendix 1 in the supplementary materials). We also evaluated swallowing difficulties and throat pain. At the end of the protocol, each subject was asked to rate preference for one or the other device, using a 5-point verbal scale ($+2$ = $HHFO_2$ much better; $+1$ = $HHFO_2$ better; 0 = no preference; -1 = $HHFO_2$ worse; -2 = $HHFO_2$ much worse) (see Appendix 2 in the supplementary materials).

Demographics and clinical data were collected at ICU admission. Treatments potentially responsible for dryness of the airway mucosa were recorded.

Statistical Analysis

Nasal caliber measurement, as correlated to nasal resistance, was the primary end point. Sample size was calculated assuming that humidification decreased nasal resistance by half.[3] In physiologic studies[3,15] it has been shown that breathing hot and humidified oxygen decreased nasal airways resistance. Assuming a square relation between resistance and 1/calibre ($R = f(1/A^2)$), with $\alpha = .05$ and $\beta = 80\%$, a total of 30 subjects were required. Qualitative data are described as number (%) and continuous data as mean ± SD, or as median and interquartile range when not normally distributed. The non-parametric Mann Whitney U test was used to compare variables. Categorical variables were analyzed using the chi-square test and using exact Fisher test for small sample. Values of $P < .05$ were considered statistically significant. Statistical analyses were performed using statistics software (PASW Statistics 18.0, SPSS, Chicago, Illinois).

Results

We prospectively included 37 subjects, who were allocated at random to standard or $HHFO_2$ groups (see Fig. 1).

Table 1. Characteristics of the Study Subjects

	Oxygen (n = 12)	$HHFO_2$ (n = 18)	P
Age, median (IQR) y	51 (39–72)	66 (45–77)	.23
SAPS II, median (IQR)	24 (12–35)	27 (22–43)	.28
Male, no. (%)	6 (50)	7 (38)	.54
Time to inclusion, median (IQR) h	24 (12–36)	12 (7–20)	.12
Body temperature, median (IQR) °C	37.8 (36.7–38.4)	37.0 (36.6–38.4)	.6
Oxygen flow at inclusion, median (IQR) L/min	9 (6–18)	12 (8–28)	.21
Oxygen device at inclusion, no. (%)			
Mask	4 (33)	10 (55)	.45
Nasal cannula	5 (42)	4 (22)	.23
$HHFO_2$	2 (17)	4 (22)	.7
Infectious pneumonia, no. (%)	4 (33)	10 (57)	.2
Acute chest syndrome, no. (%)	3 (25)	1 (5)	.3
Pulmonary embolism, no. (%)	2 (17)	1 (5)	.4
Others, no. (%)*	3 (25)	6 (33)	.3

* Cardiogenic pulmonary edema, pulmonary hypertension, acute interstitial pneumonia, hemorrhagic shock.
SAPS II = Simplified Acute Physiology Score II
$HHFO_2$ = heated humidified high-flow oxygen therapy

Among them, 7 were unable to complete the study, 5 because of clinical deterioration requiring mechanical ventilation (4 in the standard group and 1 in the $HHFO_2$ group), and 2 because of rapidly reversible respiratory failure with no need to continue oxygen therapy above 4 L/min (both in the standard oxygen group); they were not included in the analysis. Table 1 reports the main characteristics of the subjects. There were no significant differences at baseline between the groups. Oxygen requirements were similar at admission, with a median flow at 12 L/min in the $HHFO_2$ group and 9 L/min in the standard oxygen group (P = .21). The oxygen flow in the 2 groups did not change between inclusion and H24 (see Supplementary Figure 2).

At baseline (H0), minimal cross-sectional areas were similar in the 2 groups; the value increased over time in the $HHFO_2$ group, but the difference at H24 was not statistically significant (Fig. 2). The rhinometry variables did not differ significantly between the 2 groups at any time during the study.

At baseline the dryness scores at the nose, mouth, and throat were similar in the 2 groups (Fig. 3). At H4 the median nasal dryness score was significantly increased versus baseline in the standard oxygen group (6 vs 2, P = .007); it increased further in this group between H4 and H24, while it decreased in the $HHFO_2$ group (7 vs 1, respectively, P = .004). Dryness scores differed significantly between the 2 groups only for the nose (Table 2). Dryness of the mouth and throat, dysphagia, and throat pain were not significantly different between the 2 devices. A blinded evaluation by the otorhinolaryngologist could be performed at H24 in 18 subjects (10 in the $HHFO_2$ group and 8 in the standard oxygen group) and showed significantly greater nasal dryness in the standard oxygen group (P = .05).

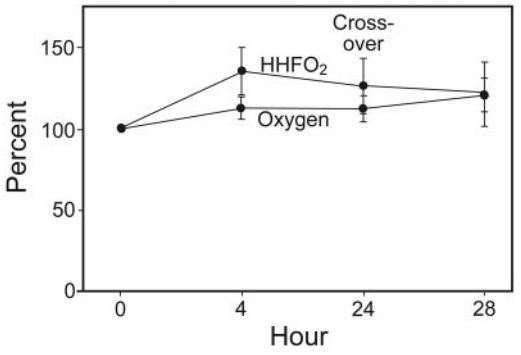

Fig. 2. Average nasal minimal cross-sectional area in all subjects. The crossover occurred at hour 24 (H24). The data are given as a percentage of the value at baseline (H0), for better understanding. Minimal cross-sectional area is thought to correlate with resistance, with lower minimal cross-sectional area being associated with higher resistance. Minimal cross-sectional area increased in the heated humidified high-flow oxygen therapy ($HHFO_2$) group, suggesting a decrease in resistance. However, there was no significant difference between the 2 groups (P = .10 at H0, P = .60 at H24, and P = .20 at H28).

At H28, 4 hours after crossover to the other device, a significantly larger number of subjects preferred $HHFO_2$ over standard oxygen (16 vs 5, P = .01), despite a relative noise induced by the device. Nine subjects expressed no preference. The subjects who preferred the $HHFO_2$ required higher oxygen flow at inclusion, compared to others (P = .05).

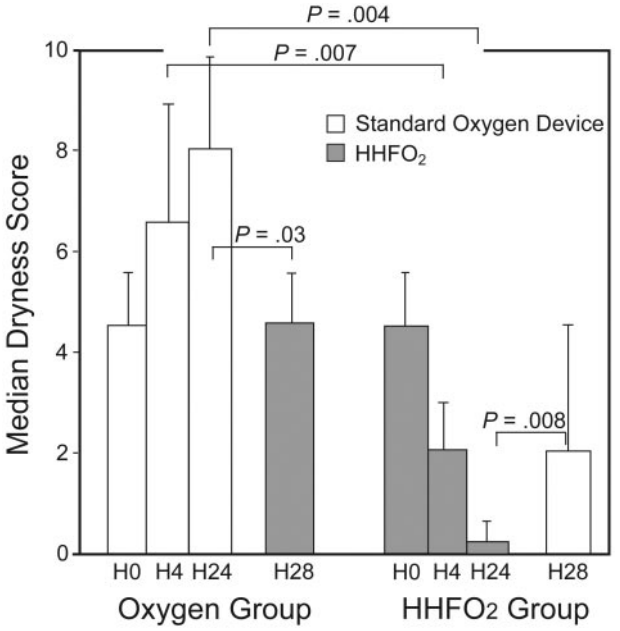

Fig. 3. Dryness score (nose) evaluated at hour 0 (H0), H4, H24, and H28, using a numerical rating scale. After 24 hours, the subjects were switched to the other device. The difference between the 2 groups was significant starting at H4 ($P = .007$). Median values and interquartile ranges are shown. $HHFO_2$ = heated humidified high-flow oxygen therapy.

Table 2. Dryness Score at Baseline and After 4, 24, and 48 Hours, as Evaluated Using a Numerical Rating Scale*

	Dryness Score, median (IQR)		
	Oxygen Group ($n = 12$)	$HHFO_2$ Group ($n = 18$)	*P*
Nose			
Hour 0	4 (0–9)	4 (1–7)	.60
Hour 4	6 (2–9)	2 (0–3)	.007
Hour 24	8 (0–10)	0 (0–2)	.004
Hour 28	4 (0–6)	2 (0–5)	.6
Throat			
Hour 0	5 (1–8)	4 (1–8)	.6
Hour 4	3 (0–8)	0 (0–4)	.2
Hour 24	0 (0–7)	0 (0–5)	.3
Hour 28	0 (0–3)	1 (0–3)	.6

* After 24 hours the subjects were switched to the other device.
$HHFO_2$ = heated humidified high-flow oxygen therapy

Discussion

A major finding from this study is that oxygen therapy delivered to critically ill patients is frequently associated with discomfort, mainly due to nasal dryness. Administering a high flow of humidified and heated oxygen markedly reduced this symptom.

The decrease in upper airway dryness seen with oxygen humidification may contribute to diminished upper-airway resistance.[15] We used acoustic rhinometry to assess airway caliber, as the minimal cross-sectional area is related to nasal resistance,[14] and found no difference between the 2 groups. However, the inter-individual variability of the rhinometry results may have impaired our ability to find an effect and to interpret the data. We do not know whether or not our study was powered enough to show such a difference or if there is a true lack of difference in airway caliber.

The impact of oxygen humidification has been documented during invasive[16–18] and noninvasive mechanical ventilation[19,20] but has not been adequately studied in spontaneously breathing patients, most notably those with hypoxemia. Several studies compared bubble humidifiers with no humidification in subjects hospitalized outside the ICU.[21,22] The difference in dryness symptoms was not significant. In a study of a bubble humidifier and a heated humidifier in the ICU, half the subjects reported moderate to severe discomfort associated with dryness of the throat and mouth, which was less marked with the heated humidifier.[12] We also found less discomfort with a heated humidifier, which was ascribable to a decrease in nasal dryness.

The improved patient comfort associated with decreased upper airway dryness is clinically relevant. In our study most of the subjects asked to continue using the $HHFO_2$ system after the study. ICU patients frequently report pain and discomfort,[2] which may be related to a variety of reasons, including care procedures and devices.[23] Discomfort adds to the many sources of stress experienced by ICU patients and may contribute to the occurrence of post-traumatic stress disorder.[24] Our study demonstrates that increasing the absolute humidity of the gas breathed spontaneously by critically ill patients with acute respiratory failure is associated with an improvement in upper airway mucosa dryness. This improvement occurred early, being significant after only 4 hours ($P = .007$). Oxygen-therapy-related airway dryness is reversible. It increased after switching from $HHFO_2$ to standard oxygen therapy and decreased after the switch in the opposite direction ($P = .008$ and $P = .03$, respectively).

Our study has limitations. First, we included subjects who needed oxygen flows above 4 L/min, which we considered as hypoxemic respiratory failure. Since we focused on the side effects of oxygen therapy, we did not have more precise entry criteria for hypoxemia. Second, after randomization we excluded 7 subjects, 6 of whom were in the standard group; 4 of these 7 subjects required mechanical ventilation before H24 in the standard group, compared to a single subject in the $HHFO_2$ group. Although this finding could suggest a beneficial effect of $HHFO_2$, our study was not designed to evaluate the impact of $HHFO_2$

on the need for mechanical ventilation. Neither did we investigate the potential impact of $HHFO_2$ on the occurrence of atelectasis, nosocomial infections, or intubation difficulties. $HHFO_2$ therapy has been shown to improve oxygenation[25] and to induce a low positive expiratory pressure in children.[26] A preliminary study in an adult cardiothoracic and vascular ICU indicated that $HHFO_2$ delivered better oxygenation than standard oxygen via a mask in patients with hypoxemic respiratory failure.[27]

The dryness scale and the declared subject preference used in our study were subjective, which constitutes a limitation of our study. However, none of the subjects had delirium. The large-print numerical scale used in our study is well suited to critically ill patients[28] and has better validity and reliability for measuring acute pain than a visual analog scale or verbal scale.[29] To minimize bias, however, we used a crossover design to ensure comparability between the 2 groups, replacing inter-subject variability by intra-subjects variability.

The main disadvantage of $HHFO_2$ reported by the subjects was the noise. Despite this increased noise, the percentage of subjects who preferred the $HHFO_2$ system was greater in the $HHFO_2$ group than in the standard oxygen group. Only 2 subjects complained of the heat generated by the $HHFO_2$ system.

Conclusions

The $HHFO_2$ system clearly improves the clinical tolerance of oxygen therapy in subjects with hypoxemic acute respiratory failure requiring high oxygen concentrations. This use should be considered early because it rapidly reduces the dryness of the nasal mucosa and decreases discomfort in most patients, despite the noise produced by the device. For spontaneously breathing patients, a true benefit may be the possibility to administer much higher flows in hypoxemic patients.

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