

High-Flow Nasal Cannula Versus Conventional Oxygen Therapy After Endotracheal Extubation: A Randomized Crossover Physiologic Study

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OBJECTIVE: Compare the short-term benefit of high-flow nasal cannula (HFNC) with non-rebreathing mask in terms of change in dyspnea, physiologic variables, and patient comfort in subjects after endotracheal extubation. **METHODS:** A randomized crossover study was conducted in a 10-bed respiratory care unit in a university hospital. Seventeen mechanically ventilated subjects were randomized after extubation to either Protocol A (applied HFNC for 30 min, followed by non-rebreathing mask for another 30 min) or Protocol B (applied non-rebreathing mask for 30 min, followed by HFNC for another 30 min). The level of dyspnea, breathing frequency, heart rate, blood pressure, oxygen saturation, and patient comfort were recorded. The results were expressed as mean \pm SD, frequency, or percentage. Categorical variables were compared by chi-square test or Fisher exact test, and continuous variables were compared by dependent or paired *t* test. Statistical significance was defined as $P < .05$. **RESULTS:** Seventeen subjects were divided into 2 groups: 9 subjects in Protocol A and 8 subjects in Protocol B. The baseline characteristics and physiologic parameters before extubation were not significantly different in each protocol. At the end of study, HFNC indicated less dyspnea ($P = .04$) and lower breathing frequency ($P = .009$) and heart rate ($P = .006$) compared with non-rebreathing mask. Most of the subjects (88.2%) preferred HFNC to non-rebreathing mask. **CONCLUSIONS:** HFNC can improve dyspnea and physiologic parameters, including breathing frequency and heart rate, in extubated subjects compared with conventional oxygen therapy. This device may have a potential role for use after endotracheal extubation. *Key words:* high-flow nasal oxygen cannula; non-rebreathing mask; endotracheal extubation; oxygen therapy-noninvasive ventilation. [Respir Care 2014;59(4):485–490. © 2014 Daedalus Enterprises]

Introduction

Oxygen therapy is essential in the management of patients who have a respiratory problem, including after en-

dotracheal extubation. Oxygen supply via face mask with bag is routinely used in these patients, but this method may be inadequate in some patients, especially if they require a high inspiratory flow (this may be from 30 L/min up to 120 L/min in patients with acute respiratory failure),¹ whereas non-rebreathing mask can provide a maximum flow of only up to 10–15 L/min. Furthermore, oxygen supply by non-rebreathing mask will be variable depending on the flow of oxygen and the patient's breathing pattern.²

High-flow nasal cannula (HFNC) is a new technological device in a high-flow oxygen system that consists of an

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air-oxygen blender, which allows from 0.21 to 1.00 F_{IO_2} and which generates a gas flow of up to 55 L/min, and a heated humidification system,³ which may have several advantages in reducing the work of breathing. This method can wash out pharyngeal dead space, reduce nasopharyngeal resistance, create some PEEP and constant F_{IO_2} , and facilitate secretion clearance from humidified gas.⁴ HFNC has been evaluated in many groups, including healthy subjects, patients with acute respiratory failure, and patients recovering from post-cardiac surgery. Extubated patients will need a high inspiratory flow and adequate oxygen supplementation, so after extubation, a high flow of oxygen may be necessary to compensate for the work of breathing; thus, HFNC may have a role in this situation via many mechanisms that have been discussed previously. However, in the medical literature, there are limited data on the benefit of HFNC in recently extubated patients. Thus, the primary objective of this study was to compare HFNC with non-rebreathing mask in extubated patients in terms of change in dyspnea, physiologic variables, and patient comfort.

Methods

Study Design and Population

A randomized, non-blinded, crossover study was conducted from August 2011 to December 2011 in a 10-bed respiratory intensive care unit in the Division of Respiratory Diseases and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand, to investigate the benefits of HFNC in terms of change in dyspnea, physiologic variables, and patient comfort and to compare them with non-rebreathing mask with bag after endotracheal extubation. This study was approved by the Siriraj Institutional Review Board and the subjects or a subject's next of kin gave informed consent.

Mechanically ventilated subjects who were ≥ 18 years of age, successfully weaned by spontaneous breathing trial (SBT) with oxygen T-piece or low level of pressure support for 120 min, and ready for endotracheal extubation were included. Subjects with hemodynamic instability or a decreased level of consciousness, subjects who lacked cooperation, tracheostomized patients, and pregnant women were excluded.

Device Description

The HFNC device (Optiflow, Fisher & Paykel Healthcare, Auckland, New Zealand) consists of an air-oxygen blender, which allows from 0.21 to 1.00 F_{IO_2} and which generates a gas flow of up to 55 L/min, and a heated humidification system (MR850 heated humidifier, Fisher & Paykel Healthcare). The gas mixture at 37°C is deliv-

QUICK LOOK

Current knowledge

High-flow nasal cannula can improve oxygenation by delivering humidified oxygen and decrease the ventilatory requirement by washing out dead space of the upper airway.

What this paper contributes to our knowledge

In a group of patients following extubation, the use of high-flow oxygen via nasal cannula reduced dyspnea and resulted in a lower breathing frequency and heart rate compared with oxygen via non-rebreathing mask.

ered via a single-limb heated inspiratory circuit to the patient through a nasal cannula. Conventional oxygen therapy was applied via a non-rebreathing mask at an oxygen flow of 6–10 L/min.

Protocol

In our respiratory ICU (with a nurse-to-patient ratio of 1:1.5 and expertise in caring for patients with respiratory problems such as acute respiratory failure and difficult weaning), weaning is guided by a non-mandatory protocol that is executed by resident trainees and pulmonologists. In general, subjects with stable hemodynamics (with mean arterial pressure ≥ 65 mm Hg and not receiving vasopressors) and adequate oxygenation ($S_{pO_2} > 92\%$ with $F_{IO_2} \leq 0.4$, PEEP ≤ 8 mm Hg, and $P_{aO_2}/F_{IO_2} \geq 150$) are weaned by SBT with oxygen T-piece or low-level pressure support for 120 min. Subjects who successfully complete the SBT are considered for endotracheal extubation.

After endotracheal extubation, the subjects were randomized into two protocols. In Protocol A, oxygen was delivered via HFNC using an initial inspiratory flow of 35 L/min, and F_{IO_2} was adjusted to achieve S_{pO_2} of at least 94% within the first 5 min and to maintain this setting for 30 min, followed by non-rebreathing mask at 6–10 L/min to achieve $S_{pO_2} \geq 94\%$ for another 30 min. We used a starting flow of 35 L/min and a study period of 30 min in each intervention based on previous studies⁵⁻⁷ that demonstrated a better performance of HFNC using a flow of 35 L/min and the detection of physiologic differences between study groups during this time period. In Protocol B, the subjects began with non-rebreathing mask for 30 min and then switched to HFNC for 30 min. After completing the study, the type and level of oxygen supplementation were adjusted by the intensive care physicians, who have this responsibility.

Data Collection

Baseline demographic and clinical data before endotracheal extubation were collected. After extubation, the level of dyspnea and patient comfort were assessed by using a visual analog scale ranging from 0 to 10. The breathing frequency, heart rate, blood pressure, and S_{pO_2} were recorded immediately after extubation and then at 5, 10, 15, and 30 min during each period of intervention. At the end of the study period, the subjects were asked whether they preferred HFNC or non-rebreathing mask.

Outcome

The primary outcome was the improved effects of HFNC in reducing dyspnea after endotracheal extubation compared with non-rebreathing mask. The secondary outcomes were effects on the physiologic variables (breathing frequency, heart rate, and mean arterial pressure) and patient comfort.

Statistical Analysis

The estimated sample size was 17 subjects based on a previous study⁵ of HFNC in acute respiratory failure, and we expected that HFNC could improve dyspnea in extubated subjects at 25% compared with non-rebreathing mask at a power of 90% with a level of significance of .05. All statistical analyses were performed using SPSS 15 (SPSS Inc., Chicago, Illinois). The results were expressed as mean \pm SD, frequency, or percentage. Categorical variables were compared by chi-square test or Fisher exact test, and continuous variables were compared by dependent or paired *t* test. Statistical significance was defined as $P < .05$.

Results

General Characteristics

Twenty-five subjects were recruited, and 17 subjects were included during the study period (8 subjects were excluded because they could not tolerate SBT for 120 min). The baseline characteristics of 17 subjects are shown in Table 1. The mean age was 66.8 ± 13.8 years, and the most common cause of respiratory failure was COPD exacerbation (6/17, 35.2%). Nine subjects were enrolled in Protocol A, and 8 subjects were enrolled in Protocol B. There were no differences in baseline characteristics and physiologic parameters before extubation between the two protocols (Table 2).

Table 1. General Characteristics

Subject, <i>n</i>	17
Age, mean \pm SD y	66.8 \pm 13.8
Male, <i>n</i> (%)	10 (58.8)
Comorbidities, <i>n</i> (%)	
Respiratory	9 (52.9)
Cardiovascular	8 (47.1)
Hypertension	8 (47.1)
Chronic kidney disease	5 (29.4)
Diabetes mellitus	5 (29.4)
Malignancy	2 (11.8)
Cerebrovascular disease	1 (5.9)
SAP II score, mean \pm SD	30.9 \pm 4.4
Etiology of respiratory failure, <i>n</i> (%)	
COPD exacerbation	6 (35.2)
Hospital-acquired pneumonia	4 (23.5)
Community-acquired pneumonia	2 (11.8)
Congestive heart failure	2 (11.8)
Massive hemoptysis	1 (5.9)
Empyema thoracis	1 (5.9)
Aspiration pneumonia	1 (5.9)
Duration of intubation, mean \pm SD d	7.1 \pm 4.4

SAPS II = Simplified Acute Physiology Score II

Table 2. Physiologic Parameters Before Extubation for Protocols A and B

Parameter	Protocol A (Mean \pm SD)	Protocol B (Mean \pm SD)	<i>P</i>
Breathing frequency, breaths/min	20.3 \pm 4.5	21.7 \pm 3.8	.98
Mean arterial pressure, mm Hg	95.1 \pm 14.1	97.6 \pm 12.9	.81
Heart rate, beats/min	93.1 \pm 8.2	88.5 \pm 8.4	.89
Oxygen saturation, %	98.5 \pm 2.9	98.4 \pm 1.7	.55

Protocol A = high-flow nasal cannula, followed by non-rebreathing mask
Protocol B = non-rebreathing mask, followed by high-flow nasal cannula

Clinical Parameters and Outcomes

The mean total gas flow in the HFNC group and that in the non-rebreathing mask group were 36.8 and 8.0 L/min, respectively. Use of HFNC was associated with significant reduction in dyspnea compared with non-rebreathing mask, and the benefit of HFNC was demonstrated at 10 min after applying the device until the end of study (Fig. 1). Dyspnea scores at 30 min after applying HFNC and non-rebreathing mask were 1.6 ± 1.2 and 2.9 ± 1.5 , respectively ($P = .04$) (Table 3).

HFNC demonstrated significant benefits in terms of heart rate and breathing frequency compared with non-rebreathing mask (Fig. 2). At the end of the study, heart rate and breathing frequency obtained with HFNC and non-rebreathing mask were 89.5 ± 9.5 and 95.4 ± 10.4 beats/

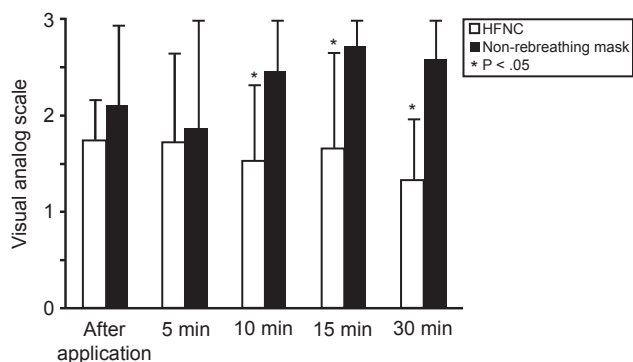


Fig. 1. Change in dyspnea. HFNC = high-flow nasal cannula

Table 3. Clinical and Physiologic Parameters for High-Flow Nasal Cannula and Non-Rebreathing Mask at the End of Intervention

Parameters	HFNC (Mean ± SD)	Non-rebreathing Mask (Mean ± SD)	P
Subjective evaluation			
Dyspnea score	1.6 ± 1.2	2.9 ± 1.5	.04*
Comfort score	1.4 ± 0.9	1.9 ± 1.1	.07
Respiratory and gas exchange variables			
Oxygen saturation, %	98.2 ± 2.1	98.8 ± 1.8	.44
Breathing frequency, breaths/min	19.8 ± 3.2	23.1 ± 4.4	.009*
Hemodynamic variables			
Mean arterial pressure, mm Hg	95.8 ± 12.3	97.5 ± 10.2	.32
Heart rate, beats/min	89.5 ± 9.5	95.4 ± 10.4	.006*

* $P < .05$

min, respectively ($P = .006$), and 19.8 ± 3.2 and 23.1 ± 4.4 breaths/min, respectively ($P = .009$). The subjects in the HFNC group were more comfortable than those in the non-rebreathing mask group, but this parameter was not significant ($P = .07$), and most of the subjects preferred HFNC rather than non-rebreathing mask (15/17, 88.2%). No significant difference in oxygen saturation and mean arterial blood pressure was found between the two groups.

Adverse Effects

There were no serious adverse effects from HFNC. Two subjects reported mild adverse effects from HFNC: the gas flow was too high, and the temperature was too warm. However, both of them tolerated HFNC until the end of the study. No subject was re-intubated or received noninvasive ventilation after completion of the study.

Discussion

This study is the first to evaluate the short-term physiologic benefits of HFNC compared with non-rebreathing mask in extubated subjects. The main results demonstrate that HFNC significantly improved dyspnea and physiologic variables in terms of breathing frequency and heart rate. Because the physiologic effects of HFNC need to be evaluated, it is difficult to translate them into clinically relevant significance. However, as most of the subjects preferred HFNC after finishing each intervention, we believe that the reported physiologic benefits of HFNC may have at least some clinical relevance.

The mechanisms of HFNC in improving outcomes after extubation are due to several factors. First, HFNC can provide the higher flow of gas that is necessary for extubated patients, who normally require high gas flow. Second, this device can create some PEEP with an average pressure of 1.5–7 cm H_2O ⁶⁻¹⁰ depending on the flow of gas; thus, it increases the functional residual capacity and improves oxygenation.¹¹ Third, the patients receive constant F_{IO_2} . Fourth, the heated humidifier can facilitate secretion clearance from the airways, protect airway epithelial cells,¹² and alleviate patient discomfort.¹³ All of these mechanisms can explain why HFNC has better outcomes compared with conventional oxygen therapy in reducing the work of breathing and improving gas exchange in patients after extubation.

HFNC has been studied mostly in pediatric patients and has shown many benefits.³ However, literature comparing this device with conventional oxygen therapy in adult patients after extubation is scant. Tiruvoipati et al¹⁴ evaluated the efficacy of HFNC by comparing it with high-flow face mask (HFFM) in extubated patients, and they found that HFNC was as effective as HFFM in delivering oxygen in terms of gas exchange, breathing frequency, and hemodynamics. In a study by Moccaldò et al¹⁵ performed with 109 subjects who were randomized to receive air-entrainment mask or HFNC, all parameters in the HFNC group were better than those in the air-entrainment mask group, and the rate of re-intubation was lower in the HFNC group. We confirm the benefits of HFNC after extubation; however, in our study, we compared HFNC with conventional oxygen therapy (low-flow system), whereas both aforementioned studies compared HFNC with the high-flow oxygen system.

The benefits of HFNC in other patient groups have been demonstrated in many clinical studies. Sztrymf et al^{16,17} found that HFNC significantly reduced breathing frequency, heart rate, dyspnea score, supraclavicular retraction, and thoraco-abdominal synchrony and increased pulse oximetry in 38 ICU patients with acute respiratory failure; this improvement was observed as early as 15 min after the beginning of HFNC. This result was consistent with

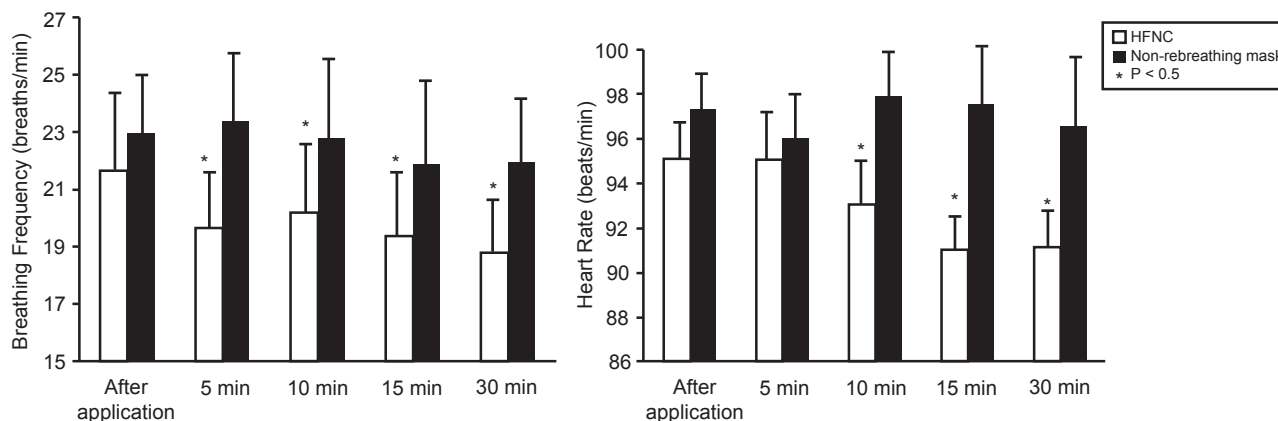


Fig. 2. High-flow oxygen via nasal cannula (HFNC) compared to non-breathing mask.

the previous study by Roca et al,⁵ who demonstrated that patients with acute respiratory failure who were treated via HFNC had better oxygenation and breathing frequency and were more comfortable than those treated via conventional oxygen face mask. Other potential indications for HFNC were exacerbation of COPD,¹⁸ post-cardiac surgery,¹⁹ during invasive procedures such as bronchoscopy,²⁰ and do-not-intubate patients.²¹

As in this study the subjects showed relatively low levels of dyspnea (dyspnea score of < 3 points), low breathing frequency (< 25 breaths/min), and low heart rate (< 100 beats/min), one could argue that similar results may have been achieved with only the conventional oxygen therapy. However, it can be reasonably speculated that greater benefits may be obtained with HFNC in patients showing greater degrees of post-extubation respiratory distress.

Limitations

This study has some limitations. First, this study could not be blinded; the protocol did not have a washout period before applying each intervention; and some baseline parameters, such as level body mass index, sedation and analgesia, were missing. Second, the actual delivered F_{IO_2} and total gas flow were not measured in the subjects who received the non-rebreathing mask because such a technique was difficult. Third, we did not measure the P_{aO_2}/F_{IO_2} ratio and P_{aCO_2} during the study. This was an important limitation in comparing gas exchange and the rebound effects on P_{aCO_2} from the oxygen therapy especially in COPD subjects. Fourth, the effect on sputum production or expectoration was not evaluated. In addition, we did not evaluate the cost-effectiveness of HFNC, and 30 min for study may not be sufficient to detect substantial physiologic differences between HFNC and conventional oxygen therapy. Thus, a large randomized study of HFNC after extubation should be performed in the future.

Conclusions

HFNC can improve dyspnea and physiologic parameters after extubation, including breathing frequency and heart rate, compared with conventional oxygen therapy. This device may have a potential role after endotracheal extubation. However, a large randomized controlled study may be required to investigate the greatest benefits of HFNC in patients after extubation.

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