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High-Flow Nasal Oxygen Cannula versus Conventional Oxygen Therapy After Endotracheal Extubation: A Randomized Cross Over Physiologic Study

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Abstract

OBJECTIVE: To compare the short term benefit of high-flow nasal oxygen cannula (HFNC) with non-rebreathing mask in terms of change of dyspnea, physiologic variables, and patient comfort in subjects after endotracheal extubation.

METHODS: A randomized cross-over 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, then followed by non-rebreathing mask for another 30 min, or Protocol B—applied non-rebreathing mask for 30 min, then followed by HFNC for another 30 min. Level of dyspnea, respiratory rate, heart rate, blood pressure, oxygen saturation, and patient comfort were recorded. The results were expressed as mean±standard deviation (SD), frequency, or percentage. Categorical variables were compared by Chi-squared test or Fisher's exact test and continuous variables were compared by dependent or pair t-test. Statistical significance was defined at $P < .05$.

RESULTS: Seventeen subjects were divided into two groups: 9 subjects were applied for protocol A whereas 8 subjects for protocol B. The baseline characteristics and physiologic parameters before extubation were not so different in each protocol. At the end of study, HFNC indicated less dyspnea ($P = .04$), lower respiratory rate ($P = .009$), and heart rate ($P = .006$) when compared with non-rebreathing mask. Most of subjects (88.2%) preferred HFNC to non-rebreathing mask.

CONCLUSIONS: HFNC can improve dyspnea and physiologic parameters in extubated subjects, including respiratory rate and heart rate when compared with conventional oxygen therapy. This device may have a potential role after endotracheal extubation.

Keywords: High-flow nasal oxygen cannula - Non-rebreathing mask - Endotracheal extubation - Oxygen therapy – Non-invasive ventilation

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Introduction

Oxygen therapy is an essential management in the patients who have a respiratory problem, including after endotracheal 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 high inspiratory flow rate (this may be from 30 L/min up to 120 L/min in patients with acute respiratory failure)[1], while the non-rebreathing mask can only provide maximum flow rate 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 oxygen cannula is a new technological device in high-flow oxygen system that consists of an air-oxygen blender (allowing from 21% to 100% FiO_2) which generates the gas flow rate up to 55 L/min and a heated humidification system[3]; this may have several advantages to reduce the work of breathing. This method can wash out pharyngeal dead space, reduce nasopharyngeal resistance, create some positive end expiratory pressure (PEEP), constant FiO_2, and facilitate secretion clearance from humidified gas[4]. HFNC has been evaluated in many groups of patients such as healthy subjects, those with acute respiratory failure, and in those recovering from post-cardiac surgery. In extubated patients, they will need the high inspiratory flow rate and adequate oxygen supplement, so after extubation high flow rate oxygen may be necessary to compensate work of breathing, thus HFNC may have a role in this situation via many mechanisms which are discussed earlier. However, in the medical literature, there are limited data about the benefit of HFNC in the recently extubated patients. Thus, the primary objective of this study is to compare HFNC with non-rebreathing mask in extubated patients in terms of change of dyspnea, physiologic variables, and patient comfort.

Methods

Study Design and Population

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

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Mechanically ventilated subjects who were age ≥ 18 years, successfully weaned by spontaneous breathing trial with oxygen T-piece or low level of pressure support for 120 minutes and ready for endotracheal extubation were included. Exclusion criteria included subjects who had hemodynamic instability, decreased level of consciousness, lack of cooperation, tracheostomized patients, and pregnant women.

Device Description

The HFNC device (Optiflow®, Fisher & Paykel, Auckland, New Zealand) consists of an air-oxygen blender allowing from 0.21 to 1.00 FiO_2 can generate gas flow rate up to 55 L/min and a heated humidification system (Fisher & Paykel, MR 850 passover humidifier). The gas mixture at 37°c is delivered via a single limb heated inspiratory circuit to the patient through nasal cannula. Conventional oxygen therapy was applied through a non-rebreathing mask at flow rate between 6-10 L/min.

Protocol

In our respiratory ICU (nurse to patient ratio is 1.5:1 and expertise in caring the patients with respiratory problem such as acute respiratory failure, difficult weaning), weaning is guided by a nonmandatory protocol that is executed by resident trainees and pulmonologists. In general, subjects who are stable hemodynamics (mean arterial pressure ≥ 65 mmHg and no receiving vasopressors), adequate oxygenation (SpO_2 > 92% with FiO_2 ≤ 0.4 and PEEP ≤ 8 mmHg and P/F ratio ≥ 150) are weaned by spontaneous breathing trial with oxygen T-piece or low level pressure support for 120 minutes. Subjects s who successfully complete the SBT are considered for endotracheal extubation.

After endotracheal extubation, the subjects were randomized into two protocols. Protocol A: oxygen was delivered via HFNC, using initial inspiratory flow rate at 35 L/min and FiO_2 was adjusted to achieve oxygen saturation (SpO_2) by pulse oximetry at least 94% within first 5 minutes and maintain this setting for 30 minutes, and then followed by non-rebreathing mask 6- 10 L/min to achieve SpO_2 ≥ 94% for another 30 minutes. The authors used the starting flow rate at 35 L/min and the study period at 30 minutes in each intervention based on the previous studies[5-7] that demonstrated a better performance of HFNC using flow rate of 35 L/min and this period could detect the physiological differences between study groups. Protocol B: the subjects were started with non-rebreathing mask for 30 minutes and then switched to HFNC for 30 minutes. After finishing the study, the type and level of oxygen supplement was adjusted by the intensive care physicians who take this responsibility.

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Data Collection

Baseline demographic and clinical data before endotracheal extubation were collected. After extubation, level of dyspnea and patient comfort were assessed by using visual analog scale ranging from 0 to 10. The respiratory rate, heart rate, blood pressure, and SpO_2 were recorded immediately after extubation and then at 5, 10, 15, and 30 minutes 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 on reducing dyspnea after endotracheal extubation as compared to non-rebreathing mask. The secondary outcomes were effects on the physiologic variables (respiratory rate, heart rate, mean arterial pressure) and patient comfort.

Statistical Analysis

The estimated sample size was 17 subjects based on the previous study[5] of HFNC in acute respiratory failure and the authors expected that HFNC can improve dyspnea in extubated subjects for 25% when compared with non-rebreathing mask with power of 90% at level of significance 0.05. All statistical analyses were performed using the SPSS software package, version 15 (Chicago, Illinois, USA). The results were expressed as mean±standard deviation (SD), frequency, or percentage. Categorical variables were compared by Chi-squared test or Fisher's exact test and continuous variables were compared by dependent or pair t-test. Statistical significance was defined at $P < .05$.

Results

General Characteristics

Twenty-five subjects were recruited and seventeen subjects were included during the study period (eight subjects were excluded because they could not tolerate spontaneous breathing trial for 120 minutes). The baseline characteristics of seventeen subjects are shown in Table 1. Mean age was 66.8±13.8 years old and the most common cause of respiratory failure was chronic obstructive pulmonary disease (COPD) exacerbation (6/17, 35.2%). Nine subjects were enrolled in protocol A and eight subjects were enrolled in protocol B. There is no difference in baseline characteristics and physiologic parameters before extubation between the two protocols (Table 2).

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Clinical Parameters and Outcomes

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

HFNC indicated the significant benefits in terms of heart rate and respiratory rate when compared with non-rebreathing mask (Fig. 2). At the end of study, heart rate and respiratory rate in HFNC and non-rebreathing mask were 89.5±9.5 and 95.4±10.4 beats per minute, respectively (P =.006) and 19.8±3.2 and 23.1±4.4, respectively (P =.009). The subjects in HFNC group were more comfortable than those with non-rebreathing mask, but this parameter was not significant (P =.07) and most of the subjects preferred HFNC rather than non-rebreathing mask (15/17 subjects; 88.2%). No significant difference in oxygen saturation and mean arterial blood pressure was found between the two groups.

Adverse Effects

There was no serious adverse effect from HFNC. Two subjects reported mild adverse effects from HFNC which were that the gas flow was too high and the temperature too warm; however, both of them tolerated HFNC until the end of the study. No subject was reintubated or received non-invasive ventilation after complete of study.

Discussion

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

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The mechanisms of HFNC in improving outcome after extubation are due to several factors. First, HFNC can provide the higher flow rate of gas that is necessary for the extubated patients who normally require high gas flow rate. Second, this device can create some positive end expiratory pressure with an average pressure of 1.5-7 cmH_2O[6-10] depends on the flow rate of gas thus it increases the functional residual capacity and improve oxygenation[11]. Third, the patients receive constant FiO_2. Fourth, the heat 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 a better outcome than conventional oxygen therapy in reducing work of breathing and improving gas exchange in the patients after extubation.

High-flow nasal oxygen cannula have been studied mostly in pediatric patients and have shown many benefits[3]. However, the evidence from the literature which compares this device with conventional oxygen therapy in adult patients after extubation is scant. Tiruvoipati et al[14] evaluated the efficacy of HFNC by comparing it with high-flow face mask (HFFM) in extubated patients and they found HFNC was as effective as HFFM in delivering oxygen in terms of gas exchange, respiratory rate, and hemodynamics. In another study by Moccaldo et al[15] of 109 subjects who were randomized to receive Venturi mask or HFNC, it was found that all parameters in the HFNC group were better than the Venturi mask and the rate of reintubation was lower in the HFNC group. We confirm the benefits of HFNC after extubation; however, our study compared HFNC with conventional oxygen therapy (low-flow system) while both of aforementioned studies compared HFNC with the high-flow oxygen system.

The benefits of HFNC in other patient groups were demonstrated in many clinical studies. In acute respiratory failure, Sztrymf et al[16, 17] found HFNC significantly reduced respiratory rate, heart rate, dyspnea score, supraclavicular retraction, thoracoabdominal synchrony, and increased pulse oximetry in thirty-eight ICU patients; this improvement was observed as early as fifteen minutes after the beginning of HFNC. This result was consistent with the previous study by Roca et al[5] which demonstrated that the patients with acute respiratory failure who were treated with HFNC had better oxygenation, respiratory rate, and more comfortable than those with conventional oxygen face mask. Other potential indications for HFNC were acute 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 values of dyspea (dyspnea scale lower than 3 points), respiratory rate (under 25 breaths per minute), and heart rate (under 100 beats per minute), one could argue that similar results may have been achieved with the only conventional oxygen therapy. However, it could

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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 wash out period before applying each intervention, and we have some missing baseline parameters such as level body mass index, sedation and analgesia. Second, the actual delivered FiO_2 and total gas flow rate were not measured in the subjects who received the non-rebreathing mask because such a technique was difficult. Third, the authors did not measure the PaO_2/FiO_2 ratio and $PaCO_2$ during the study; thus this was the important limitation in comparing the gas exchange and the rebound effects on $PaCO_2$ from the oxygen therapy especially in COPD subjects. Fourth, the effect on sputum production or expectoration was not evaluated. In addition, the authors did not evaluate the cost-effectiveness of HFNC and the period of study at 30 minutes may not be sufficient to detect substantial physiologic differences between HFNC and conventional oxygen therapy. Thus, a large randomized study for HFNC after extubation should be further evaluated in the future.

Conclusion

High-flow nasal oxygen cannula can improve dyspnea and physiologic parameters after extubation, including respiratory rate and heart rate when compared to conventional oxygen therapy. This device may have a potential role after endotracheal extubation. However, a large randomized control study may be required to investigate the greatest benefits of HFNC in patients after extubation.

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Fig. 1. Change of Dyspnea by Visual Analog Scale (VNS). * $P<.05$

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Fig. 2. Change of Respiratory Rate (A) and Heart Rate (B). * $P<.05$

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Table 1. Geneal Characteristics

Subject (*n*)	17
Age (mean±SD *y*)	66.8±13.8
Male (*n, %*)	10 (58.8)
Comorbidities (*n, %*)	
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±SD)	30.9±4.4
Etiology of respiratory failure (*n, %*)	6 (35.2)
COPD exacerbation	4 (23.5)
Hospital acquired pneumonia	2 (11.8)
Community acquired pneumonia	2 (11.8)
Congestive heart failure	1 (5.9)
Massive hemoptysis	1 (5.9)
Empyema thoracis	1 (5.9)
Aspiration pneumonia	
Duration of intubation (mean±SD *days*)	7.1±4.4

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Table 2. Physiologic Parameters Before Extubation Between Protocol A and B

	Protocol A (mean±SD)	Protocol B (mean±SD)	*P*
Respiratory rate (*per minute*)	20.3±4.5	21.7±3.8	0.98
Mean arterial pressure (*mmHg*)	95.1±14.1	97.6±12.9	0.81
Heart rate (*beat per minute*)	93.1±8.2	88.5±8.4	0.89
Oxygen saturation (*%*)	98.5±2.9	98.4±1.7	0.55

Protocol A: high flow nasal oxygen cannula then non-rebreathing mask

Protocol B: non-rebreathing mask then high flow nasal oxygen cannula

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Table 3. Clinical and Physiologic Parameters in HFNC and Non-rebreathing Mask at the End of Intervention.

	HFNC (mean±SD)	Non-rebreathing Mask (mean±SD)	*P*
Subjective evaluation			
- Dyspnea scale	1.6±1.2	2.9±1.5	0.04*
- Comfort scale	1.4±0.9	1.9±1.1	0.07
Respiratory and gas exchange variables			
- Oxygen saturation (*%*)	98.2±2.1	98.8±1.8	0.44
- Respiratory rate (*per minute*)	19.8±3.2	23.1±4.4	0.009*
Hemodynamic variables			
- Mean arterial pressure (*mmHg*)	95.8±12.3	97.5±10.2	0.32
- Heart rate (*per minute*)	89.5±9.5	95.4±10.4	0.006*

* $P<.05$

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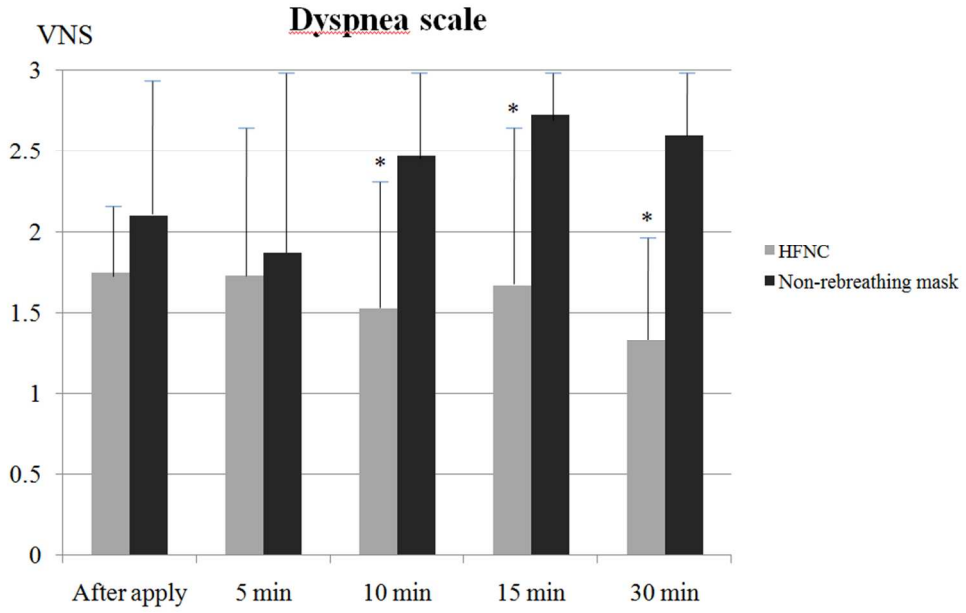

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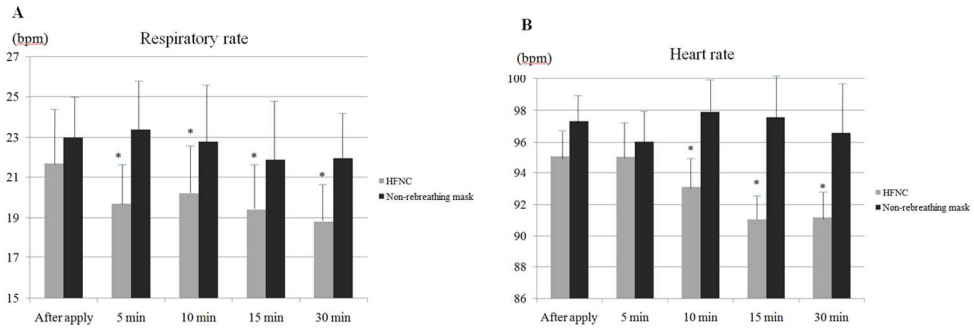

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