

Use of High-Flow Nasal Cannula for Acute Dyspnea and Hypoxemia in the Emergency Department

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BACKGROUND: Acute dyspnea and hypoxemia are 2 of the most common problems in the emergency room. Oxygen therapy is an essential supportive treatment to correct these issues. In this study, we investigated the physiologic effects of high-flow nasal oxygen cannula (HFNC) compared with conventional oxygen therapy (COT) in subjects with acute dyspnea and hypoxemia in the emergency room. **METHODS:** A prospective randomized comparative study was conducted in the emergency department of a university hospital. Forty subjects were randomized to receive HFNC or COT for 1 h. The primary outcome was level of dyspnea, and secondary outcomes included change in breathing frequency, subject comfort, adverse events, and rate of hospitalization. **RESULTS:** Common causes of acute dyspnea and hypoxemia were congestive heart failure, asthma exacerbation, COPD exacerbation, and pneumonia. HFNC significantly improved dyspnea (2.0 ± 1.8 vs 3.8 ± 2.3 , $P = .01$) and subject comfort (1.6 ± 1.7 vs 3.7 ± 2.4 , $P = .01$) compared with COT. No statistically significant difference in breathing frequency was found between the 2 groups at the end of the study. HFNC was well tolerated, and no serious adverse events were found. The rate of hospitalization in the HFNC group was lower than in the COT group, but there was no statistically significant difference (50% vs 65%, $P = .34$). **CONCLUSIONS:** HFNC improved dyspnea and comfort in subjects presenting with acute dyspnea and hypoxemia in the emergency department. HFNC may benefit patients requiring oxygen therapy in the emergency room. *Key words:* high-flow nasal oxygen cannula; oxygen therapy; dyspnea; hypoxemia; emergency room. [Respir Care 2015;60(10):1377–1382. © 2015 Daedalus Enterprises]

Introduction

Acute dyspnea with accompanying hypoxemia is a major problem in emergency departments. Common causes of this condition include acute pulmonary edema, pneu-

monia, and exacerbation of chronic obstructive airway diseases such as asthma and COPD. Specific therapy for the underlying disease is the mainstay of treatment. However, oxygen therapy is an essential supportive treatment to correct hypoxemia and alleviate breathlessness.¹ Oxygen supply via a nasal cannula or non-rebreathing mask is routinely used, but these methods may be inadequate to support patients' increased work of breathing, particularly if they require a high inspiratory flow (range of 30–120 L/min in acute respiratory failure).² Furthermore, variations in F_{IO_2} occur with conventional oxygen therapy (COT), and delivered F_{IO_2} depends on oxygen flow and the patient's breathing pattern.³

High-flow nasal cannula (HFNC) is a heated, humidified, high-flow oxygen delivery system that can generate

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total gas flows of up to 60 L/min with an adjustable F_{IO_2} .⁴ This device can provide some PEEP that may help to improve oxygenation and counteract the effects of intrinsic PEEP on work of breathing and that may act by washing out oropharyngeal dead space.⁵ It may also help to reduce inspiratory resistance and facilitate secretion clearance from humidified gas.⁴ HFNC has demonstrated benefits in terms of improving dyspnea and oxygenation in subjects with acute respiratory failure,⁶ after endotracheal extubation,⁷ and in post-cardiac surgery subjects.⁸ In addition, a recent study demonstrated that subjects receiving HFNC after extubation had a lower re-intubation rate compared with subjects receiving standard oxygen therapy.⁹ However, the benefit of HFNC for patients with acute dyspnea and hypoxemia in the emergency department is limited. Thus, the aim of this study was to compare the physiologic effects of HFNC versus COT on subjects with acute dyspnea and hypoxemia in an emergency department.

Methods

Subjects and Study Design

A prospective randomized comparative study (Thai Clinical Trials Registry identifier TCTR20140618002) was conducted from May 2012 to November 2012 in an emergency department of the Faculty of Medicine Siriraj Hospital in Bangkok, Thailand, to investigate the effects of HFNC in terms of physiologic changes (dyspnea, breathing frequency, oxygenation, and comfort), adverse events, and hospitalization rate compared with COT in subjects with acute dyspnea and hypoxemia. This study was approved by the Siriraj institutional review board (protocol 041/2555[EC1]), and subjects or their relatives provided informed consent.

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The study enrolled subjects ≥ 18 y old who developed acute dyspnea with hypoxemia (breathing frequency > 24 breaths/min and $S_{pO_2} < 94\%$ on room air). Subjects with hemodynamic instability, need for invasive mechanical ventilation, chronic respiratory failure with long-term oxygen supplementation, decreased level of consciousness (Glasgow Coma Scale score < 13), and lack of cooperation or who were pregnant were excluded.

Device Description

The HFNC device (Optiflow, Fisher & Paykel Healthcare, Auckland, New Zealand) consists of an air-oxygen blender that can generate air-oxygen flow of up to 60 L/min with F_{IO_2}

QUICK LOOK

Current knowledge

Heated-and-humidified O_2 delivered by high-flow nasal cannula reduces ventilatory requirements by flushing the anatomic dead space and improves oxygenation by meeting inspiratory flow demands. A low level of end-expiratory pressure may also be generated, further enhancing oxygenation. Heat and humidity allow high flows to be tolerated and improve patient comfort.

What this paper contributes to our knowledge

Heated-and-humidified high-flow O_2 resulted in less dyspnea and better comfort compared with conventional O_2 therapy (COT) in subjects presenting to the emergency room with acute dyspnea and hypoxemia. Mean O_2 flow was 35 L/min in the high-flow group and 6 L/min in the COT group. There were no differences in hospital admission rates between the groups.

adjusted between 0.21 to 1.00 and heated humidification (MR850 pass-over humidifier, Fisher & Paykel Healthcare). The air-oxygen mixture at 37°C was delivered via a single-limb heated inspiratory circuit through a nasal cannula. COT was applied through a nasal cannula or a non-rebreathing mask per emergency physician preference.

Protocol

The eligible subjects were randomized into 2 groups with a blind envelope pull. In the HFNC group, oxygen was delivered at an inspiratory flow of 35 L/min, and F_{IO_2} was adjusted to achieve an S_{pO_2} of $\geq 94\%$ within the first 5 min and was continued for 60 min. In the COT group, oxygen was supplied via a nasal cannula or non-rebreathing mask at a flow of 3–10 L/min to maintain an S_{pO_2} of $\geq 94\%$ for 60 min.

Data Collection

Baseline demographic and clinical data were collected. Physiologic variables, including breathing frequency, heart rate, mean arterial pressure, and S_{pO_2} , were recorded immediately after applying each intervention and then at 5, 10, 15, 30, and 60 min. Dyspnea levels and subject comfort were assessed using a numerical rating scale ranging from 0 to 10.¹⁰ Hospital admission rate, adverse events, and other specific adjunctive treatments such as diuretics, inhaled medication, systemic corticosteroids, and antibiotics were recorded.

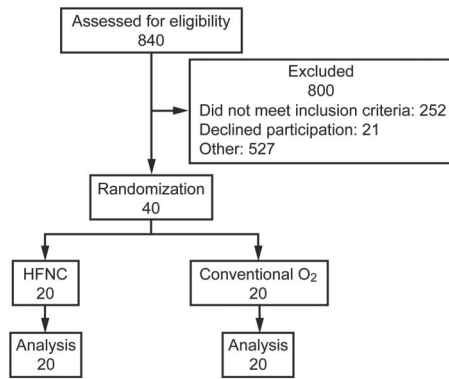


Fig. 1. Flow chart. HFNC = high-flow nasal cannula.

Outcome Variables

The primary outcome was the effect of HFNC on dyspnea levels compared with COT. The secondary outcomes were the effects on breathing frequency, other physiologic variables (mean arterial pressure and heart rate), subject comfort, adverse events, and hospitalization rate.

Statistical Analysis

On the basis of a previous study on HFNC in acute respiratory failure,⁶ we expected that HFNC would improve dyspnea by 25% in subjects with acute dyspnea and hypoxemia compared with COT. Assuming a 2-sided α value of .05, the estimated sample size was 38 subjects with a power of 90%. Data were analyzed with an intention-to-treat approach. All statistical analyses were performed using SPSS 18 (SPSS, Chicago, Illinois). The results were expressed as mean \pm SD, frequency, or percentage. Normality of the distribution was assessed with the Kolmogorov-Smirnov test. Categorical variables were compared by chi-square tests. For changes in continuous variables between groups (time effect of 0–60 min), a mixed between/within-subject analysis of covariance (using age, variable at baseline, bronchodilator, and corticosteroid as covariates), followed by a post hoc test, was performed. Missing data for a subject in the HFNC group due to withdrawal from the study and a subject in the COT group due to a technical issue were addressed using an expectation-maximization technique. $P < .05$ was considered statistically significant.

Results

Baseline Characteristics

Forty subjects were enrolled in this study (Fig. 1). One subject in the HFNC group withdrew immediately after applying the device due to intolerance, and one

subject in the COT group had missing data because of a technical issue. The mean age was 64.6 ± 14.9 y, and the mean Acute Physiology and Chronic Health Evaluation II score was 15.1 ± 3.5 . Baseline characteristics were similar between the 2 groups, except the heart rate in the HFNC group was lower than in the COT group (93.5 ± 16.2 vs 107.7 ± 24.0 beats/min, $P = .04$) (Table 1). Common causes of acute dyspnea and hypoxemia were congestive heart failure, pneumonia, and asthma and COPD exacerbations. No difference in the emergency department diagnosis or co-treatment was found between the 2 groups.

Clinical Parameters and Outcomes

Mean total air-oxygen flow and F_{IO_2} in the HFNC group were 35.5 ± 2.2 L/min and 0.45 ± 0.09 , respectively. In the COT group, oxygen was delivered at a mean total flow of 5.6 ± 3.0 L/min. HFNC significantly improved the level of dyspnea compared with COT. This effect was demonstrated as early as 5 min after applying the HFNC up through the end of the study, except at 30 min (Fig. 2). At the end of the study, subjects who received HFNC had a better comfort level compared with those who received COT. HFNC significantly reduced breathing frequency during the study period (from 10 to 30 min), although no significant difference in breathing frequency was found between the 2 groups at the end of the study. The heart rate in the HFNC group was significantly lower compared with the COT group at the end of the study. No significant differences in mean arterial pressure and S_{pO_2} were observed between the 2 groups (Table 2).

Adverse Events and Hospitalization Rate

No serious adverse events occurred. Three subjects in the HFNC group reported minor events: unpleasant smell, too warm temperature, and chest discomfort. No subject was intubated or received noninvasive ventilation. There was a downward trend in the rate of hospitalization in the HFNC group compared with the COT group, but this difference was not statistically significant (50% vs 65%, $P = .34$).

Discussion

To our knowledge, this is the first randomized study to compare HFNC and COT in the emergency department. The main outcome demonstrated that HFNC significantly improved the level of dyspnea and that this effect was immediate. This finding was consistent with other studies on subjects with acute respiratory failure. Roca et al⁶ compared HFNC and COT in a randomized cross-over study and demonstrated that HFNC improved dyspnea and com-

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Table 1. Baseline Characteristics of the Groups of Randomized Subjects

Characteristic	HFNC (n = 20)	COT (n = 20)	P
Age, mean ± SD y	65.6 ± 14.4	63.6 ± 15.7	.26
Females, n (%)	11 (55.0)	14 (70.0)	.51
Underlying disease, n (%)			
Cardiovascular	7 (35.0)	3 (15.0)	.14
Respiratory	8 (40.0)	10 (50.0)	.38
Diabetes mellitus	5 (25.0)	9 (45.0)	.16
Hypertension	10 (50.0)	10 (50.0)	.62
Other	5 (25.0)	6 (30.0)	.50
Diagnosis in emergency department, n (%)			
Congestive heart failure	9 (45.0)	5 (25.0)	.16
Asthmatic attack	2 (10.0)	5 (25.0)	.20
COPD exacerbation	3 (15.0)	2 (10.0)	.50
Pneumonia	3 (15.0)	6 (30.0)	.23
Other	3 (15.0)	2 (10.0)	.50
Co-treatment, n (%)			
Diuretics	8 (40.0)	5 (25.0)	.25
Bronchodilators	12 (60.0)	14 (70.0)	.37
Corticosteroids	7 (35.0)	7 (35.0)	.63
Antibiotics	4 (20.0)	5 (25.0)	.50
Initial physiologic parameters			
Breathing frequency, mean ± SD breaths/min	31.7 ± 5.5	32.1 ± 5.0	.81
Mean arterial pressure, mean ± SD mm Hg	100.4 ± 22.9	104.6 ± 16.9	.51
Heart rate, mean ± SD beats/min	93.5 ± 16.2	107.7 ± 24.0	.04
S _{pO₂} , mean ± SD %	85.9 ± 9.0	88.7 ± 4.5	.23

HFNC = high-flow nasal oxygen cannula
COT = conventional oxygen therapy

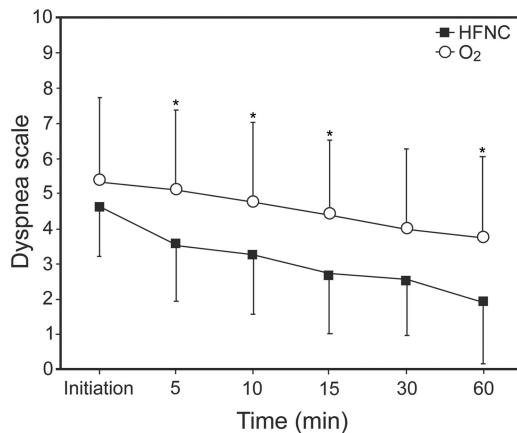


Fig. 2. Change in level of dyspnea assessed using a numerical rating scale (0–10) between high-flow nasal cannula (HFNC) and conventional oxygen therapy. HFNC significantly improved dyspnea as early as 5 min after application, and this effect continued to the end of the study, except at 30 min. * $P < .05$.

fort. In addition, HFNC was better tolerated and provided better comfort compared with COT. An observational study by Lenglet et al¹¹ showed that HFNC decreased dyspnea scores compared with COT in subjects with acute respiratory failure presenting to an emergency department. Fur-

thermore, Schwabbauer et al¹² found that HFNC significantly reduced dyspnea and improved comfort compared with noninvasive ventilation in subjects with hypoxemic respiratory failure. In addition, the subjects in the present study tolerated HFNC very well, and no serious adverse events occurred during the study period. Furthermore, subjects who received HFNC trended toward reduced hospitalization, but this was not found to be statistically significant.

Improvement of dyspnea by HFNC can be explained by several mechanisms, including the high gas flow matching subjects' demand,¹³ decreased pharyngeal dead space,^{5,14,15} low levels of positive airway pressure,¹⁶⁻¹⁹ improved thoracoabdominal synchrony,²⁰ and reduced symptoms of mucosal dryness with heated-and-humidified gas.²¹⁻²³ In addition, all of these mechanisms also explain why HFNC improved gas exchange and subject comfort. The advantage of HFNC in terms of improving dyspnea, subject comfort, and oxygenation has also been noted in other subject populations, such as post-cardiac surgery⁸ and post-endotracheal extubation subjects,^{7,9} and during fiberoptic bronchoscopy.²⁴

Several studies demonstrated that HFNC reduced breathing frequency and also improved oxygenation in subjects

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Table 2. Comparing Clinical and Physiologic Parameters for the HFNC and COT Groups at the End of the Study

Parameter	HFNC	COT	P
Dyspnea scale score, mean ± SD	2.0 ± 1.8	3.8 ± 2.3	.01
Breathing frequency, mean ± SD breaths/min	26.0 ± 6.2	27.5 ± 4.9	.82
Mean arterial pressure, mean ± SD mm Hg	88.7 ± 10.9	101.0 ± 24.8	.31
Heart rate, mean ± SD beats/min	91.7 ± 19.3	101.6 ± 24.2	.04
S _{pO₂} , mean ± SD %	96.8 ± 2.5	97.6 ± 2.0	.13
Comfort scale score, mean ± SD	1.6 ± 1.7	3.7 ± 2.4	.01

HFNC = high-flow nasal oxygen cannula
COT = conventional oxygen therapy

with acute respiratory failure.²⁵⁻²⁸ In the present study, we found that HFNC significantly reduced breathing frequency during the study period, but there was no significant difference at the end of the study. This could be explained by the effect of specific treatments such as bronchodilator medications or diuretics, which had time to act and modified the pathophysiology of the subjects' presentation.²⁹⁻³³

Patients receiving HFNC should be closely monitored using parameters similar to those used during noninvasive ventilation. Messika et al³⁴ found that HFNC failure was associated with lower P_{aO₂}/F_{IO₂} and higher breathing frequency and Simplified Acute Physiology Score II. In addition, in a retrospective observational study on subjects with acute respiratory failure, Kang et al³⁵ found that HFNC failure led to delayed endotracheal intubation and worse clinical outcomes. In the present study, no subject was intubated or received noninvasive ventilation because they were less sick compared with the subjects in the above-mentioned studies. Thus, appropriate selection and frequent re-evaluation of patients during HFNC use will help to improve outcomes, particularly in the emergency department.

This study has some limitations. First, there was a 1.5-h delay on average between the screening period and protocol initiation. Second, we did not measure delivered F_{IO₂} in the COT group because this technique was difficult to perform in the emergency department. Third, arterial blood gases were not measured during the study. This was an important limitation for comparing gas exchange between the 2 groups and the potential changes in P_{aCO₂} from oxygen therapy, particularly in subjects with COPD.

Conclusions

In conclusion, HFNC resulted in less dyspnea and better comfort in comparison with COT in subjects presenting to the emergency department with acute dyspnea and hypoxemia. This device may benefit patients requiring oxygen therapy in the emergency department.

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