Original Article

High-Flow Nasal Cannula for Patients with Acute Respiratory Failure Treated in a General Medical Ward: A Prospective Cohort Study

Nuttapol Rittayamai MD[1], Prach Chuariyakul MD[2], Nattapol Promlee MSc[1], Prasit Chailard BSc[1], Nitipatana Chierakul MD[1], Laurent Brochard MD, PhD[3,4]

[1] Division of Respiratory Diseases and Tuberculosis, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

[2] Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

[3] Keenan Research Centre, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada

[4] Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, Ontario, Canada

Background: Hypoxemia and the need for oxygen administration are frequent causes of hospital admission. High-flow nasal cannula (HFNC) delivers heated humidified high-flow gas at an adjustable inspired oxygen fraction via a large-bore nasal cannula and provide specific physiological benefits. The efficacy of HFNC has been investigated in the intensive care unit but data in other care settings are scarce, especially in low- and middle-income countries.

Objective: To describe the safety and associated clinical outcomes of HFNC used in patients admitted to general medical wards.

Materials and Methods: The present study was a prospective cohort study that enrolled adult patients with acute respiratory failure and no other major organ failures admitted to the general medical wards at Siriraj Hospital in Bangkok and treated with HFNC. Enrolled subjects were managed by a multidisciplinary care team trained in HFNC usage. The primary outcome was to determine the rate of HFNC failure, defined as the subsequent need for endotracheal intubation, non-invasive ventilation (NIV), reintubation, or death within 48 hours. Secondary outcomes included determining the in-hospital mortality, 28-day mortality, and the factors associated with HFNC failure.

Results: Seventy-one subjects were enrolled. In these patients, acute de novo hypoxemic respiratory failure was the most common indication for HFNC (42.3%), followed by prophylaxis after extubation (38.0%), and cardiogenic pulmonary edema (19.7%). The overall rate of HFNC failure was 25.4%. The overall in-hospital and 28-day mortality rates were 14.1% and 21.1%, respectively. The only factor associated with HFNC failure was the respiratory rate at day 1.

Conclusion: The use of HFNC in general medical wards is feasible, but a 25% rate of failure within 48 hours can be expected. A higher respiratory rate at day 1 is associated with the failure of HFNC.

Keywords: Acute respiratory failure; General medical ward; High-flow oxygen therapy; Outcomes; Safety

Received 3 March 2021 | Revised 5 May 2021 | Accepted 14 May 2021

J Med Assoc Thai 2021;104(7):1179-86

Website: http://www.jmatonline.com

Oxygen therapy is a mainstay supportive treatment in patients with acute hypoxemic respiratory failure. Oxygen-delivery systems can be broadly categorized as low-flow and high-flow systems[1]. Conventional low-flow oxygen therapy via a simple nasal cannula or an oxygen mask, with or without reservoir bag, is commonly used as an important component of the initial management of patients with hypoxemia. However, these devices can provide a maximum flow rate of only 10 to 15 liters per minute (L/minute), which might be insufficient to meet the demand of patient with acute hypoxemic respiratory failure and increase work of breathing. In addition, the fraction of inspired oxygen (FiO_2) may become variable due to the dilution of oxygen from room air entrainment[2].

Oxygen therapy via a high-flow nasal cannula (HFNC) is a high-flow oxygen-delivery system that can deliver a heated and humidified air-oxygen gas mixture with a maximum flow rate of up to 60 L/minute via a large-bore nasal cannula. The FiO_2 can

Correspondence to:

Rittayamai N.

Division of Respiratory Diseases and Tuberculosis, Department of Medicine Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand.

Phone: +66-2-4197757 ext. 11, **Fax**: +66-2-4197760

Email: nuttapol.rit@mahidol.ac.th

How to cite this article:

Rittayamai N, Chuariyakul P, Promlee N, Chailard P, Chierakul N, Brochard L. High-Flow Nasal Cannula for Patients with Acute Respiratory Failure Treated in a General Medical Ward: A Prospective Cohort Study. J Med Assoc Thai 2021;104:1179-86.

doi.org/10.35755/jmedassocthai.2021.07.12689

be adjusted from 21% to 100%[3]. HFNC offers several physiological and clinical benefits in critically ill patients with acute hypoxemic respiratory failure from various etiologies in the intensive care unit (ICU)[4-7]. HFNC has also been shown to reduce the likelihood of respiratory failure after extubation compared to conventional oxygen therapy in patients at low risk of extubation failure[8]. Furthermore, HFNC was found not to be inferior to non-invasive ventilation (NIV) in patients at high risk of extubation failure[9], and in post-cardiac surgery patients[10].

HFNC is now also employed outside the ICU[11,12]. Several studies have reported that HFNC is feasible and effective for improving gas exchange and breathing patterns in patients in the emergency department (ED)[13-15]; however, a benefit of HFNC on clinical outcomes was not observed in a large randomized clinical trial[16]. The general medical ward is another setting where oxygen delivery by HFNC is increasingly being used, especially in low- and middle-income settings. In the present study hospital, many patients with acute hypoxemic respiratory failure have been treated with HFNC in the general medical wards due to shortage of ICU beds during their admission. However, data specific to the effectiveness of HFNC in a general medical ward setting are scarce.

Objective

The aim of the present study was to describe the clinical outcomes and safety of patients with acute respiratory failure treated with HFNC in the general medical wards of Siriraj Hospital, Bangkok, Thailand, the largest national tertiary referral center, and to identify the factors associated with the failure of HFNC.

Materials and Methods

Study design and subjects

The present research involved a prospective cohort study conducted between October 2017 and March 2018 in the general medical wards at the Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. Adult patients, over 18 years old, who were admitted to any of eight general medical wards and received HFNC for at least 24 hours were enrolled in the study. Due to the limitations of ICU beds in the authors' hospital, patients with acute hypoxemic respiratory failure and patients after extubation, who had stable hemodynamics, normal level of consciousness, and no need for renal replacement therapy, were considered for admission to the general medical wards, with the actual location determined by the hospital bed manager. The types, settings, and indications of oxygen therapy were considered by the attending physician. Each ward had a capacity of 20 beds located in one large room, where all the patients were visible from the nursing station, with a nurse-to-patient ratio of 1:4 during the day shift and 1:6 during the night shift. Patients were taken care of and continuously monitored by a multidisciplinary team, including internal medicine physicians, which were one attending staff, one 3rd-year resident, and two 1st-year residents, and nurses trained in and familiar with the HFNC device. The present study was conducted in accordance with the Declaration of Helsinki and approved by the Siriraj Institutional Review Board (certificate of approval #Si 525/2017). Written informed consent to participate was obtained from each subject or their relatives.

Device description

The HFNC device (Airvo-2™; Fisher & Paykel Healthcare, Auckland, New Zealand) consists of a flow generator up to 60 L/minute, an air-oxygen blender that can adjust the FiO_2 from 21% to 100%, and an auto-fill MR 290 heated chamber. The air-oxygen mixture was delivered at 34°C to 37°C via a single-limb heated breathing circuit to the subject via an Optiflow™ nasal cannula (Fisher & Paykel, Auckland, New Zealand). The settings of the HFNC, including temperature, flow rate, and FiO_2, are clinically adjusted and modified by the attending physician based on the status of each subject.

Data collection

The patients' baseline demographic and clinical data, including age, gender, comorbidity, Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores (using the worst variable within 24 hours before the initiation of HFNC), cause of hospital admission, and indication for HFNC use, were collected and recorded. The other data collected included the duration of HFNC use, the daily recorded setting of the HFNC device, the patient's vital signs, oxygen saturation by pulse oximetry (SpO_2), and the ROX index (defined as the ratio of SpO_2/FiO_2 to the respiratory rate)[17] at 9:00 a.m. during the first three days of HFNC use.

Outcomes

The primary outcome was determining the rate

of HFNC failure, which was defined as a subsequent requirement for endotracheal intubation, NIV, reintubation, or death within 48 hours of HFNC use. The secondary outcomes were in-hospital mortality and 28-day mortality. The authors categorized the study subjects into three groups according to the indication for HFNC as 1) subjects with acute de novo hypoxemic respiratory failure admitted directly to the ward, 2) post-extubation prophylaxis for extubation failure, and 3) subjects with cardiogenic pulmonary edema. The authors performed analyses to evaluate the outcomes of the HFNC in each category, and analyzed the factors independently associated with HFNC failure.

Statistical analysis

Normally distributed variables were expressed herein as the mean ± standard deviation and analyzed by independent t-test. Non-normally distributed variables were expressed as median [interquartile range] and analyzed by Mann-Whitney U test. Normality of the data distribution was tested by Kolmogorov-Smirnov test. Categorical variables were presented as frequency and percentage and analyzed by chi-square test. Univariate and multivariate backward stepwise logistic regression analyses were used to identify the factors significantly associated with HFNC failure, and those results were shown as odds ratio and 95% confidence interval. Data were analyzed using PASW Statistics, version 18.0 (SPSS Inc., Chicago, IL, USA). A p-value of less than 0.05 was considered statistically significant.

Results

Seventy-one subjects were enrolled in the present study. The mean age of the subjects was 71±15 years old, 46.5% of them were male, and the mean APACHE II and SOFA scores were 17±6 and 6±3, respectively. The other baseline characteristics and physiologic variables before HFNC use are presented in Table 1.

Pneumonia was the leading cause of hospital admission (53.5%), followed by extra-pulmonary infection (14.1%), and congestive heart failure (12.7%). The types of oxygen therapy before initiating HFNC were a simple oxygen cannula (38.0%), invasive mechanical ventilation (38.0%), oxygen mask with a reservoir bag (22.5%), and NIV (1.5%) (Table 1).

Table 1. Baseline demographic and clinical characteristics of subjects treated with high-flow nasal cannula

Variables	n=71; n (%)
Age (years); mean±SD	71±15
Sex: male	33 (46.5)
Body mass index (kg/m^2); mean±SD	24.8±6.4
Comorbidity	
Hypertension	48 (67.6)
Cardiovascular disease	31 (43.7)
Diabetes	29 (40.8)
Chronic kidney disease	23 (32.4)
Neurological disease	15 (21.1)
Malignancy	11 (15.5)
Hematologic disease	11 (15.5)
Chronic respiratory disease	10 (14.1)
Receiving immunosuppressive drugs	9 (12.7)
APACHE II score; mean±SD	17±6
SOFA score; mean±SD	6±3
Diagnosis on admission	
Pneumonia	38 (53.5)
Extrapulmonary infection	10 (14.1)
Congestive heart failure	9 (12.7)
Malignancy	4 (5.6)
Others	10 (14.1)
Type of oxygen therapy before HFNC use	
Low-flow nasal cannula	27 (38.0)
Invasive mechanical ventilation	27 (38.0)
Oxygen mask with reservoir	16 (22.5)
Non-invasive ventilation	1 (1.5)

APACHE II=Acute Physiologic and Chronic Health Evaluation II; HFNC=high-flow nasal cannula; SD=standard deviation; SOFA=Sequential Organ Failure Assessment; SpO_2=oxygen saturation by pulse oximetry

HFNC use

On day 1, the median [interquartile range] flow rate, FiO_2, and temperature were 40 [40 to 50] L/minute, 0.40 [0.40 to 0.40], and 34 [34 to 34] °C, respectively. The mean duration of HFNC use in the present study was 61 [25 to 109] hours.

According to the pre-specified HFNC subgroups, 42.3% of subjects had acute de novo hypoxemic respiratory failure with most of these were pneumonia, 38.0% post-extubation prophylaxis, and 19.7% cardiogenic pulmonary edema.

Clinical outcomes

The overall rate of HFNC failure within 48 hours was 25.4%. Among the 18 subjects who failed HFNC, increased work of breathing and worsening hypoxemia were the reasons described for the failure of HFNC (94.4%), whereas the development of hypercapnia presented in only 5.6% of subjects who failed HFNC.

Table 2. Comparison of the demographic, anthropometric, and clinical variables between subjects with high-flow nasal cannula success and failure

Variables	HFNC success (n=53); mean±SD	HFNC failure (n=18); mean±SD	p-value
Age (years)	71±15	71±17	0.949
Body mass index (kg/m^2)	24.6±6.7	25.3±5.5	0.713
APACHE II score	17±6	19±7	0.098
SOFA score	6±3	6±2	0.548
Baseline clinical parameters			
MAP (mmHg)	88±14	93±11	0.152
RR (breaths/minute)	27±4	29±5	0.113
HR (beats/minute)	105±16	113±15	0.055
SpO_2 (%)	96±2	95±3	0.016
HFNC settings on day 1; median [IQR]			
Flow rate (L/minute)	40 [40 to 50]	40 [40 to 50]	0.598
FiO_2	0.40 [0.40 to 0.45]	0.40 [0.40 to 0.40]	0.159
Temperature (°C)	34 [34 to 34]	34 [34 to 34]	0.737
Clinical parameters on day 1 of HFNC			
RR (breaths/minute)	23±4	26±4	0.002
SpO_2 (%)	96±4	95±3	0.183
ROX index	10.45±2.31	9.86±3.20	0.402
MAP (mmHg)	89±13	88±15	0.691
HR (beats/minute)	94±19	107±20	0.016
Duration of HFNC use (hours); median [IQR]	70 [35 to 112]	37 [4 to 42]	0.001

APACHE II=Acute Physiologic and Chronic Health Evaluation II; FiO_2=fraction of inspired oxygen fraction; HFNC=high-flow nasal cannula; HR=heart rate; IQR=interquartile range; MAP=mean arterial blood pressure; RR=respiratory rate; SD=standard deviation; SOFA=Sequential Organ Failure Assessment; SpO_2=oxygen saturation by pulse oximetry

A p-value of less than 0.05 was considered statistically significant

The in-hospital and 28-day mortality rates were 14.1% and 21.1%, respectively. Subjects who failed HFNC had a significantly higher respiratory rate and heart rate at day 1 compared to subjects with HFNC success. Other variables comparing between the subjects with HFNC success and failure are shown in Table 2.

According to the indication for HFNC use, the rates of HFNC failure in subjects with acute de novo hypoxemic respiratory failure, post-extubation prophylaxis, and cardiogenic pulmonary edema were 40.0%, 18.5%, and 7.1%, respectively (Figure 1). The other clinical outcomes and type of respiratory support after failure of HFNC are shown in Table 3.

Overall adverse events of HFNC in the present study occurred in 7.0% of cases. All those events were minor, including an uncomfortably warm temperature and excessive noise.

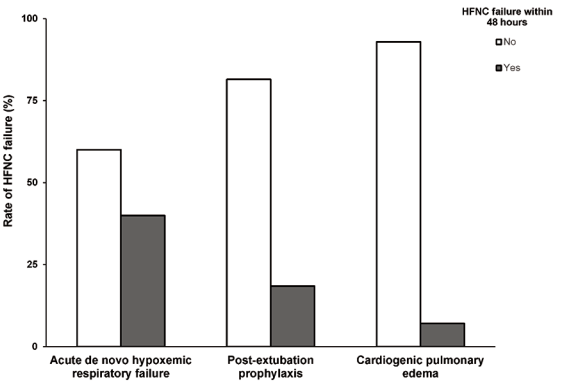

Figure 1. Rate of failure according to the indications for high-flow nasal cannula (HFNC) use.

Factors associated with the failure of HFNC

Overall, 18 subjects failed HFNC and needed the escalation of respiratory support to NIV or endotracheal intubation. No serious adverse events, such as catastrophic intubation or sudden cardiac arrest, occurred in subjects who failed HFNC. In-hospital mortality between HFNC success and failure was 3.8% versus 44.4%, respectively (p<0.001).

The authors compared the subjects with early

Table 3. Clinical outcomes of high-flow nasal cannula use in general medical wards

	Acute de novo hypoxemic respiratory failure (n=30); n (%)	Post-extubation prophylaxis (n=27); n (%)	Cardiogenic pulmonary edema (n=14); n (%)
Rate of HFNC failure within 48 hours	12 (40.0)	5 (18.5)	1 (7.1)
Duration of HFNC use (hours); median [IQR]	42 [15 to 97]	69 [37 to 109]	88 [25 to 148]
Type of respiratory support after HFNC failure			
Endotracheal intubation	11 (91.7)	4 (80.0)	1 (100.0)
Non-invasive ventilation	1 (8.3)	1 (20.0)	0 (0.0)
Length of hospital stay (days); median [IQR]	18 [11 to 28]	26 [11 to 35]	17 [13 to 27]
In-hospital mortality	6 (20.0)	3 (11.1)	1 (7.1)
28-day mortality	9 (30.0)	3 (11.1)	3 (21.4)
Adverse event	1 (3.3)	2 (7.4)	2 (14.3)

HFNC=high-flow nasal cannula; IQR=interquartile range

Table 4. Univariate and multivariate logistic regression analyses for factors independently associated with the failure of HFNC

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
APACHE II	1.05	0.93 to 1.17	0.437			
Baseline HR	1.02	0.97 to 1.07	0.397			
Baseline SpO_2	0.92	0.70 to 1.19	0.509			
HFNC indication	1.22	0.30 to 4.91	0.783			
RR at day 1	1.17	0.98 to 1.40	0.077	1.26	1.07 to 1.50	0.007
HR at day 1	1.01	0.97 to 1.05	0.578			
SpO_2 at day 1	0.96	0.82 to 1.13	0.617			

APACHE II=Acute Physiologic and Chronic Health Evaluation II; CI=confidence interval; HFNC=high-flow nasal cannula; HR=heart rate; OR=odds ratio; RR=respiratory rate; SpO_2=oxygen saturation by pulse oximetry

or 48 hours or less, and late HFNC failure or more than 48 hours, and found no significant difference in in-hospital mortality between the two groups (40.0% versus 66.7%, respectively, p=0.396). The authors searched for factors associated with the failure of HFNC using logistic regression analysis. Multivariate analysis showed only a higher respiratory rate at day 1 to be significantly associated with HFNC failure (Table 4).

Discussion

In the present prospective cohort study, the authors evaluated the clinical outcomes and safety of HFNC use in 71 subjects admitted to the general medical wards at Siriraj Hospital. The primary outcome demonstrated that the rate of HFNC failure within 48 hours was 25.4%, and the secondary outcomes showed in-hospital and 28-day mortality rates of 14.1% and 21.1%, respectively. The authors also classified subjects who received HFNC into three groups, namely acute de novo hypoxemic respiratory failure from various etiologies, post-extubation prophylaxis for extubation failure, and subjects with cardiogenic pulmonary edema, and found the highest rate of HFNC failure and in-hospital mortality in the subjects with acute de novo hypoxemic respiratory failure.

High-flow oxygen therapy has been extensively investigated in critically ill patients in the ICU. Several physiological and clinical studies have reported that HFNC significantly reduced the respiratory rate, improved oxygenation, and reduced the work of breathing compared to conventional oxygen therapy in patients with acute hypoxemic respiratory failure[4,6,18,19]. The physiological benefits of HFNC can be explained by mechanisms that include the generation of positive end-expiratory pressure[20-22], alteration of nasopharyngeal resistance[23], washing out of the airway dead space[24], and the effect of heat and humidification to relieve dryness and to preserve airway mucosal function[25,26]. HFNC has been evaluated in several large, randomized control studies in subjects with acute respiratory failure who received HFNC for various indications. A study by Frat et al[27] comparing HFNC, conventional oxygen therapy, and NIV in subjects with acute hypoxemic respiratory failure found that the overall intubation rate did not significantly differ among the three groups, however, subjects who had moderate-to-severe hypoxemia had a significantly lower rate of endotracheal intubation compared to in conventional oxygen therapy and NIV. Furthermore, subjects treated with HFNC had a significant lower mortality rate at 90 days compared to the other two groups. A large, randomized study by Stephan et al[10] reported that HFNC did not significantly differ from NIV in subjects with acute

respiratory failure after cardiothoracic surgery in terms of both treatment failure and ICU mortality. HFNC has also been evaluated for its ability to prevent respiratory failure after endotracheal extubation. A randomized study by Maggiore et al[28] found better comfort, less cases of oxygen desaturation, and a lower intubation rate in subjects who were treated with HFNC compared to the Venturi mask. Two other large randomized clinical trials demonstrated that HFNC reduced the risk of reintubation within 72 hours compared to conventional oxygen therapy in subjects at low risk of needing intubation[8], and that HFNC was not inferior to NIV for preventing post-extubation respiratory failure and reintubation in subjects at high risk of needing intubation[9].

HFNC is now being increasingly used in settings outside of the ICU, such as in the ED[29]. Many studies conducted in the ED have found HFNC to be feasible for use in patients with acute hypoxemic respiratory failure, but the effect of HFNC on patients' outcomes, such as the rate of intubation and hospitalization, is still questionable[13-16,30]. The general medical ward is another setting where HFNC is being increasingly used, especially in patients receiving palliative care[31-33]. However, there is little data to support its safety and efficacy in this setting, in particular in patients without a "do-not-resuscitate" order. Moreover, there is a risk using HFNC in general medical wards, with less monitoring than in the ICU as it may delay the escalation of respiratory support or intubation in patients who fail HFNC. A study by Pirret et al[34] evaluated the use of HFNC in 67 adult subjects with respiratory failure or at risk of respiratory deterioration admitted in the general medical ward and found improved oxygen saturation and lowered respiratory rate and heart rate in patients after HFNC had been applied for 20 minutes. The overall mortality rate at hospital discharge was 10.4%[34]. However, the included subjects in that study were less sick as determined by the SOFA score compared to the present study. A recent short-term observational study by Zemach et al[35] demonstrated that implementing HFNC for 30 minutes in 111 subjects with acute hypoxemic respiratory failure treated outside the ICU, including in intermediate care units, and general medical, geriatric, and hemato-oncology wards, significantly improved the level of dyspnea, breathing pattern, and oxygenation. However, the overall mortality rate in that study was 50%, and the mortality rate remained high after excluding subjects with a "do-not-resuscitate" order (30%).

To the best of the authors knowledge, the present study is the first study to evaluate the long-term outcomes of HFNC use in patients with acute hypoxemic respiratory failure from various conditions admitted to a general medical ward in the context of a low- to middle-income country with limited resources. Many patients developed acute hypoxemic respiratory failure in the authors' department had to be managed in general medical wards due to the limited availability of ICU beds during their admission. The mortality rate at hospital discharge was lower in the present study than in a previous study[35]. Furthermore, the HFNC failure and mortality rates in the present study were similar to those from other studies conducted in ICUs with similar patient severity[9,10,27]. Interestingly, subjects who experienced HFNC success had almost zero mortality, while subjects who failed HFNC had a high mortality rate, but comparable to patients with acute respiratory distress syndrome who failed NIV in the LUNG SAFE study[36]. The authors found a trend toward an increase in mortality in subjects with late HFNC failure of more than 48 hours. The present study finding was similar to a previous retrospective study demonstrating a worse outcome in subjects with delayed intubation after the failure of HFNC[37]. The authors believe that an appropriate training program to comprehensively familiarize all attending staff, residents, nurses, and respiratory therapists with the HFNC device should be mandatory before the adoption and implementation of an HFNC system. In addition, appropriate monitoring during HFNC use is important and the escalation of respiratory support should not be delayed in patients with clinical deterioration.

The present study logistic regression analyses revealed that only a higher respiratory rate at day 1 was significantly associated with the failure of HFNC. However, the number of subjects who failed HFNC in the present study was small. Another study with larger sample size is needed to confirm the results. Another index, the so-called ROX index, which is the ratio of SpO_2/FiO_2 to the respiratory rate, has been previously evaluated for its ability to identify intubation risk among patients with acute hypoxemic respiratory failure who were known to be at risk for intubation[38]. A study by Roca et al[17] reported that a ROX index of 4.88 or higher at 2, 6, and 12 hours after the initiation of HFNC was significantly associated with a lower risk of intubation. In the present study, the authors did not find that the ROX index was associated with HFNC failure, but the authors did not collect all the required ROX index-related data at those same time

points as in the previous study[17].

Limitation

The present study has some important limitations to note. First, the study was a single-center study, and it was not a randomized controlled trial. Second, the study was conducted in a single university hospital, and the physicians, nurses, and respiratory therapists were well-trained in and familiar with the use of the HFNC device. Third, different management strategies will potentially influence the results. In addition, the nurse-to-patient ratio was still compatible with minimal monitoring, especially because there were no single room, and the patients were all together. Therefore, the subjects were always 'visible' to the nurses. This suggests that the present study findings might not be generalizable to all healthcare settings and patient populations. Further well-designed studies are needed to demonstrate the benefits of the use of HFNC outside the ICU.

Conclusion

The use of HFNC in subjects with acute respiratory failure in general medical wards is feasible. A higher respiratory rate at day 1 is associated with a higher risk of failure of HFNC. Appropriate patient selection and monitoring are needed to the success of HFNC.

What is already known on this topic?

Oxygen therapy via a HFNC has been demonstrated to provide several physiological and clinical benefits in critically ill patients with acute hypoxemic respiratory failure in the ICU. Now, it is increasingly being used outside the ICU, however, the knowledge of safety and effectiveness of HFNC in such places are scarce.

What does this study add?

Treatment with HFNC in patients with acute hypoxemic respiratory failure and in high-risk patients after extubation in general medical wards is feasible. Appropriate monitoring during HFNC use is needed to prevent the failure of HFNC. Early detection and the prompt escalation of respiratory support in patients with failure of HFNC may improve the clinical outcome.

Acknowledgement

The authors would like to thank Miss Khemajira Karaketklang of the Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, and Mr. Suthipol Udompunthurak of the Clinical Epidemiology Unit, Research Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, for their assistance with the statistical analyses.

Conflicts of interest

Laurent Brochard's laboratory has over time received equipment or research grants from Medtronic Covidien (PAV), Air liquide (CPR), Philips (sleep), Sentec ($tcPCO_2$), Fisher & Paykel (high-flow therapy), and General Electric (lung volume). The other authors have no conflicts of interest to declare.

References

1. Kallstrom TJ. AARC clinical practice guideline: oxygen therapy for adults in the acute care facility--2002 revision & update. Respir Care 2002;47:717-20.
2. O'Driscoll BR, Howard LS, Earis J, Mak V. BTS guideline for oxygen use in adults in healthcare and emergency settings. Thorax 2017;72(Suppl 1):ii1-90.
3. Ricard JD. High flow nasal oxygen in acute respiratory failure. Minerva Anestesiol 2012;78:836-41.
4. Mauri T, Turrini C, Eronia N, Grasselli G, Volta CA, Bellani G, et al. Physiologic effects of high-flow nasal cannula in acute hypoxemic respiratory failure. Am J Respir Crit Care Med 2017;195:1207-15.
5. Papazian L, Corley A, Hess D, Fraser JF, Frat JP, Guitton C, et al. Use of high-flow nasal cannula oxygenation in ICU adults: a narrative review. Intensive Care Med 2016;42:1336-49.
6. Roca O, Riera J, Torres F, Masclans JR. High-flow oxygen therapy in acute respiratory failure. Respir Care 2010;55:408-13.
7. Rochwerg B, Granton D, Wang DX, Helviz Y, Einav S, Frat JP, et al. High flow nasal cannula compared with conventional oxygen therapy for acute hypoxemic respiratory failure: a systematic review and meta-analysis. Intensive Care Med 2019;45:563-72.
8. Hernández G, Vaquero C, González P, Subira C, Frutos-Vivar F, Rialp G, et al. Effect of postextubation high-flow nasal cannula vs conventional oxygen therapy on reintubation in low-risk patients: A randomized clinical trial. JAMA 2016;315:1354-61.
9. Hernández G, Vaquero C, Colinas L, Cuena R, González P, Canabal A, et al. Effect of postextubation high-flow nasal cannula vs noninvasive ventilation on reintubation and postextubation respiratory failure in high-risk patients: A randomized clinical trial. JAMA 2016;316:1565-74.
10. Stéphan F, Barrucand B, Petit P, Rézaiguia-Delclaux S, Médard A, Delannoy B, et al. High-flow nasal oxygen vs noninvasive positive airway pressure in hypoxemic patients after cardiothoracic surgery: A randomized clinical trial. JAMA 2015;313:2331-9.
11. Ricard JD, Roca O, Lemiale V, Corley A, Braunlich J, Jones P, et al. Use of nasal high flow oxygen

during acute respiratory failure. Intensive Care Med 2020;46:2238-47.
12. Rochwerg B, Einav S, Chaudhuri D, Mancebo J, Mauri T, Helviz Y, et al. The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. Intensive Care Med 2020;46:2226-37.
13. Rittayamai N, Tscheikuna J, Praphruetkit N, Kijpinyochai S. Use of high-flow nasal cannula for acute dyspnea and hypoxemia in the emergency department. Respir Care 2015;60:1377-82.
14. Macé J, Marjanovic N, Faranpour F, Mimoz O, Frerebeau M, Violeau M, et al. Early high-flow nasal cannula oxygen therapy in adults with acute hypoxemic respiratory failure in the ED: A before-after study. Am J Emerg Med 2019;37:2091-6.
15. Makdee O, Monsomboon A, Surabenjawong U, Praphruetkit N, Chaisirin W, Chakorn T, et al. High-flow nasal cannula versus conventional oxygen therapy in emergency department patients with cardiogenic pulmonary edema: A randomized controlled trial. Ann Emerg Med 2017;70:465-72.e2.
16. Jones PG, Kamona S, Doran O, Sawtell F, Wilsher M. Randomized controlled trial of humidified high-flow nasal oxygen for acute respiratory distress in the emergency department: The HOT-ER study. Respir Care 2016;61:291-9.
17. Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G, et al. An index combining respiratory rate and oxygenation to predict outcome of nasal high-flow therapy. Am J Respir Crit Care Med 2019;199:1368-76.
18. Vargas F, Saint-Leger M, Boyer A, Bui NH, Hilbert G. Physiologic effects of high-flow nasal cannula oxygen in critical care subjects. Respir Care 2015;60:1369-76.
19. Sztrymf B, Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D, et al. Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intensive Care Med 2011;37:1780-6.
20. Parke R, McGuinness S, Eccleston M. Nasal high-flow therapy delivers low level positive airway pressure. Br J Anaesth 2009;103:886-90.
21. Parke RL, McGuinness SP. Pressures delivered by nasal high flow oxygen during all phases of the respiratory cycle. Respir Care 2013;58:1621-4.
22. Corley A, Caruana LR, Barnett AG, Tronstad O, Fraser JF. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. Br J Anaesth 2011;107:998-1004.
23. Mündel T, Feng S, Tatkov S, Schneider H. Mechanisms of nasal high flow on ventilation during wakefulness and sleep. J Appl Physiol (1985) 2013;114:1058-65.
24. Möller W, Celik G, Feng S, Bartenstein P, Meyer G, Oliver E, et al. Nasal high flow clears anatomical dead space in upper airway models. J Appl Physiol (1985) 2015;118:1525-32.
25. Cuquemelle E, Pham T, Papon JF, Louis B, Danin PE, Brochard L. Heated and humidified high-flow oxygen therapy reduces discomfort during hypoxemic respiratory failure. Respir Care 2012;57:1571-7.
26. Spoletini G, Alotaibi M, Blasi F, Hill NS. Heated humidified high-flow nasal oxygen in adults: Mechanisms of action and clinical implications. Chest 2015;148:253-61.
27. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. N Engl J Med 2015;372:2185-96.
28. Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F, et al. Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. Am J Respir Crit Care Med 2014;190:282-8.
29. Bell N, Hutchinson CL, Green TC, Rogan E, Bein KJ, Dinh MM. Randomised control trial of humidified high flow nasal cannulae versus standard oxygen in the emergency department. Emerg Med Australas 2015;27:537-41.
30. Epstein AS, Hartridge-Lambert SK, Ramaker JS, Voigt LP, Portlock CS. Humidified high-flow nasal oxygen utilization in patients with cancer at Memorial Sloan-Kettering Cancer Center. J Palliat Med 2011;14:835-9.
31. Hui D, Morgado M, Chisholm G, Withers L, Nguyen Q, Finch C, et al. High-flow oxygen and bilevel positive airway pressure for persistent dyspnea in patients with advanced cancer: a phase II randomized trial. J Pain Symptom Manage 2013;46:463-73.
32. Koyauchi T, Hasegawa H, Kanata K, Kakutani T, Amano Y, Ozawa Y, et al. Efficacy and tolerability of high-flow nasal cannula oxygen therapy for hypoxemic respiratory failure in patients with interstitial lung disease with do-not-intubate orders: A retrospective single-center study. Respiration 2018;96:323-9.
33. Pirret AM, Takerei SF, Matheson CL, Kelly M, Strickland W, Harford J, et al. Nasal high flow oxygen therapy in the ward setting: A prospective observational study. Intensive Crit Care Nurs 2017;42:127-34.
34. Zemach S, Helviz Y, Shitrit M, Friedman R, Levin PD. The use of high-flow nasal cannula oxygen outside the ICU. Respir Care 2019;64:1333-42.
35. Bellani G, Laffey JG, Pham T, Madotto F, Fan E, Brochard L, et al. Noninvasive ventilation of patients with acute respiratory distress syndrome. Insights from the LUNG SAFE study. Am J Respir Crit Care Med 2017;195:67-77.
36. Kang BJ, Koh Y, Lim CM, Huh JW, Baek S, Han M, et al. Failure of high-flow nasal cannula therapy may delay intubation and increase mortality. Intensive Care Med 2015;41:623-32.
37. Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard JD, et al. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: The utility of the ROX index. J Crit Care 2016;35:200-5.