Original Article

ISSN: 1735-0344 *Tanaffos 2024; 23(2): 156-162*

TANAFFOS

High-Flow Nasal Cannula versus Conventional Oxygen Therapy for Patients with Acute Respiratory Failure in the Emergency Department: A Randomized Controlled Trial

Mohammad Emami Ardestani [1], Mohammad Nasr-Esfahani [2], Fatemeh Sadat MirMohammad Sadeghi [1], Reza Azizkhani [2], Farhad Heydari [2]

[1] Department of Internal Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; [2] Department of Emergency Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Received: 13 May 2023
Accepted: 18 March 2024

Correspondence to: MirMohammad Sadeghi FS
Address: Department of Internal Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
Email address: drfm.sadeghi@gmail.com

Background: To compare the efficacy of a high-flow nasal cannula (HFNC) versus conventional oxygen therapy (COT) in the treatment of patients admitted to the emergency department (ED) for acute respiratory failure (ARF).
Materials and Methods: In this prospective randomized clinical trial, 66 patients aged 18 years or older who presented with ARF to the ED were enrolled and assigned into two equal groups to receive either COT or HFNC for 60 minutes. The primary outcome was the intubation rates. The secondary outcomes were the effect of intervention on oxygenation, ICU admission rate, and effect on physiologic variables.
Results: 33 patients were treated in each group. The main causes of ARF were chronic obstructive pulmonary disease (COPD), pneumonia, and asthma. The need for intubation was higher in COT than in HFNC (42.5% vs 12.1%, P = 0.004). Patients with HFNC had a higher dyspnea improvement than those treated with COT (93.9% vs 63.7%, P = 0.002). They also showed greater improvement in oxygen saturation (increase in SpO_2 was 8.3% vs. -0.5, difference 8.8% (6.8 to 10.9)), and in respiratory rate (decrease 3.0 beats/min vs 0.2 beats/min, differences 2.8(0.8 to 4.6)). The ICU admission was higher in the COT group (51.5 vs 15.2, P=0.002).
Conclusion: HFNC reduced the need for intubation and ICU admission in the patients presenting to the ED with ARF compared with COT. In addition, HFNC was associated with a greater reduction in RR and improvement in SpO_2 compared with COT.

Keywords: Emergency department; Dyspnea; Acute respiratory failure; High-flow nasal cannula; Oxygen

INTRODUCTION

Acute dyspnea is a major problem and is commonly presented in the emergency department (ED) (1,2). Acute respiratory failure (ARF) is one of the critical conditions presented to the ED and is a major cause of admission into the ICU (1,3). The in-hospital mortality rate of ARF was 20.6% in the United States in 2009 and 42.1% of patients with ARF required mechanical ventilation (MV), which is associated with a significant increase in the length of hospital stay (4). Common causes of ARF include cardiogenic pulmonary edema, pneumonia, and acute exacerbation of chronic obstructive pulmonary diseases (COPD) or asthma (5,6).

Underlying disease and oxygen therapy is the mainstay of treatment for ARF. Usual first-line treatment includes oxygen therapy to correct hypoxemia and alleviate

breathlessness (2,7). Conventional oxygen therapy (COT) delivered via nasal cannula or non-rebreathing mask is routinely used but, these methods have several drawbacks including limited and lack of delivery of high and controlled inspired fractions of oxygen (FiO_2), insufficient heating and humidifying, and poor tolerance (1,2,8). The maximal flow rate of COT devices is 15 L/min, which is not enough for patients with ARF (range of 30 –120 L/min). Also, these flow rates may be significantly lower than the inspiratory flow rate of patients and this leads to dilution of inhaled oxygen with room air (9). Furthermore, FiO_2 delivered with COT is variable.

The high-flow nasal cannula (HFNC) is another oxygen-delivering method gaining increasing attention among clinicians. HFNC is an emerging technology designed to allow for airflows as high as 50–60 L/min to achieve inspired FiO_2 as high as 95–100% with an optimal degree of heat and humidification offers patients comfort during the therapy while high flow washes out physiologic dead space and generates positive end expiration pressure (PEEP), which leads to a reduced respiratory effort and improved oxygenation. The warm and humidified oxygen facilitates mucociliary clearance, helps expectoration, decreases bronchospasm, and maintains mucosal functions. HFNC could decrease the interruption of oxygen therapy in patients (e.g., during eating, drinking, or talking) and increase patient compliance, therefore potentially improving outcomes.

The benefits of HFNC have been reported to a limited extent in patients admitted to ED due to ARF, but no such study has been performed in the Iranian population. This study aimed to compare the efficacy of high-flow nasal cannula versus conventional oxygen therapy in the treatment of patients admitted to the ED for acute hypoxemic respiratory failure.

MATERIALS AND METHODS

Study design and setting

This prospective, un-blinded, randomized controlled trial was conducted from May 2019 to November 2020 in the ED of Al-Zahra Hospital, Isfahan, Iran. The study was approved by the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1399.249) and was registered in the Iranian Registry of Clinical Trials under the number IRCT20181203041838N2. The subjects or their relatives provided written informed consent for participation in the trial.

Study population

Eligible patients were adults aged 18 years or older, who presented to the ED with acute hypoxemic respiratory failure. Inclusion criteria were: an oxygen saturation by pulse oximetry (SpO_2) of less than 90% despite additional standard oxygen for at least 15 min, a respiratory rate of >25 breaths/min, or the use of accessory muscles to breathe and abdominal asynchrony.

Patients with hemodynamic instability, need for immediate endotracheal intubation, diagnosis of cardiogenic pulmonary edema, a Glasgow Coma Scale (GCS) score less than 13, pregnancy, obesity hypoventilation syndrome, lack of cooperation, and contraindications to the use of positive airway pressure devices were excluded.

Interventions

The eligible patients were given oxygen therapy via nasal cannula for at least 15 min. If the SpO_2 was still less than 90%, the patients were included in the study. After written informed consent was obtained, patients were randomized with a computer-generated, mixed-block (block size of 2 and 4) into two groups, to receive either conventional oxygen therapy (COT group) or high-flow nasal cannula (HFNC group) for 60 min.

In the HFNC group, oxygen was delivered at an initial inspiratory flow of 35 L/min, which could be adjusted from 30 to 60 L/min according to the participant's level of comfort. The FiO_2 and flow rate were adjusted to maintain SpO_2 greater than or equal to 95% within the first 5 min and was continued for 60 min. Subjects were given HFNC by an Optiflow cannula using an AIRVO 2 humidified high-flow system (Fisher & Paykel Healthcare, Auckland, New Zealand). In the COT group, oxygen was delivered

via a nasal cannula or non-rebreathing mask at a maximum flow rate of 10 –15 L/min. The flow rate was adjusted to maintain $SpO_2 \geq 95\%$ for 60 min. After 60 min, the chosen method for oxygen therapy, the need for intubation, and transfer to the ICU were assessed by the physician.

In each group, subjects were monitored in the ED for at least 2 h, and during and after the trial, all of them received standard treatment to alleviate respiratory distress at the discretion of the treating physician.

Data Collection

Baseline characteristics (gender and age), cause of respiratory failure, and clinical data were collected. Physiologic variables including respiratory rate (RR), heart rate (HR), systolic and diastolic blood pressure (SBP and DBP), and SpO_2 were assessed immediately after inclusion and then at 15, 30, and 60 min after initiation of intervention. Arterial blood gases were checked and collected after applying each intervention and then at 60 min.

The patient's dyspnea improvement and satisfaction were recorded using a 5-point Likert scale (marked improvement, slight improvement, no change, slight deterioration, or marked deterioration) 60 min after applying each intervention (1). The intubation rate and need for ICU admission were also recorded.

Outcome Measures

The primary outcome was the intubation rates of both of the groups. The secondary outcomes were the effect of the intervention on oxygenation, ICU admission rate, the effect on physiologic variables, and the patient's dyspnea improvement and satisfaction.

Statistical Analysis

The sample size was calculated by assuming that 50% of patients would have improved dyspnea after 60 min. The estimated sample size was 28 patients with a 2-sided type I error of 0.05, and 80% power. Thus, the study population of 33 subjects in each group was calculated for an anticipated dropout rate of 20% to ensure an adequately powered study.

All statistical analyses were performed using SPSS 25 (Chicago, Illinois). Quantitative and qualitative variables were expressed as mean ± SD, frequency, or percentage. Categorical variables were compared using the chi-square tests. Continuous variables were compared using the Student's t-test or the Mann-Whitney U test. Paired t-test was used to compare changes before and after the intervention. A repeated-measures analysis of variance was used to test the difference between the two groups in terms of physiologic variables. A P value < 0.05 was considered statistically significant.

RESULTS

Study population

During the study period, 97 patients presented to the ED with acute hypoxemic respiratory failure. Of these, 31 patients were excluded for the following reasons: cardiogenic pulmonary edema (n = 16), GCS < 13 (n = 7), hemodynamic instability (n = 4), and immediate endotracheal intubation (n = 4). A total of 66 subjects were included and underwent randomization.

The mean age was 66.9 ± 12.9 years, and most of the included subjects were male (71.2%). Baseline and respiratory state characteristics of participants were similar in both groups, except the HCO3 in the HFNC group was higher than in the COT group (25.2 ± 6.9 vs 33.0 ± 16.1, P = 0.014) (Table 1). The main causes of ARF were chronic obstructive pulmonary disease (COPD), pneumonia, and asthma.

Outcomes

The COT group was associated with a higher proportion of patients who needed intubation during the study period (42.5% in COT vs 12.1% in the HFNC group, P=0.004).

The analysis of physiologic parameters demonstrated a significant difference in RR, and HR at baseline and 60 min in the HFNC group, but these parameters did not change significantly in the COT group (Table 2). Patients who received HFNC showed significant improvement in oxygen saturation with an increase in SpO_2 of 82.2% to

90.5% 60 min after treatment initiation (differences 8.3% (95%CI,6.7 to 9.9)), although no significant difference in SpO_2 was found in the COT group. $PaCO_2$ in the HFNC group decreased significantly between baseline and 60 min (48.8 mmHg versus 44.1 mmHg, difference 4.7 mmHg (95%CI, 1.9 to 7.5)). Changes in physiological and ABG parameters and comparisons between the two groups are shown in Table 2.

Table 1. Baseline characteristics and clinical data of the patients

	All patients (n = 66)	HFNC group (n = 33)	COT group (n = 33)	P-value
Age, years	66.9 ± 12.9	64.7 ± 11.7	69.2 ± 13.9	0.167
Gender, no. (%)				
Male	47 (71.2)	25 (75.8)	22 (66.7)	0.415
Female	19 (28.8)	8 (24.2)	11 (33.3)	
Cause of respiratory failure, no. (%)				
COPD exacerbation	28 (42.4)	15 (45.5)	13(39.4)	
Pneumonia	18 (27.3)	7 (21.2)	11 (33.3)	0.730
Asthmatic attack	15 (22.7)	8 (24.2)	7 (21.2)	
Others	5 (7.7)	3 (9.1)	2 (6.1)	
Initial physiologic parameters				
Respiratory rate	24.4 ± 6.2	24.2 ± 6.6	24.6 ± 5.8	0.767
Heart rate	87.3 ± 12.8	86.3 ± 12.0	88.2 ± 13.7	0.557
Systolic blood pressure	130.7 ± 13.5	129.9 ± 12.0	131.5 ± 15.0	0.626
Diastolic blood pressure	80.9 ± 11.6	80.8 ± 11.2	81.1 ± 12.2	0.925
SpO_2	82.5 ± 6.0	82.2 ± 5.3	82.8 ± 6.6	0.699
Admitted to ICU, no (%)	22 (33.3)	5 (15.2)	17 (51.5)	0.002
Intubation rate, no (%)	18 (27.3)	4 (12.1)	14 (42.4)	0.004
Initial arterial blood gas parameters				
PH	7.32 ± 0.11	7.33 ± 0.08	7.31 ± 0.13	0.389
PaCO2	44.8 ± 19.7	48.3 ± 18.8	41.4 ± 20.2	0.162
HCO3	29.1 ± 13.0	25.2 ± 6.9	33.0 ± 16.1	0.014
Patients improvement after 60 min, no (%)				
Marked improvement	22(33.3)	17(51.5)	5(15.2)	
Slight improvement	30(45.5)	14(42.4)	16(48.5)	0.002
No change	11(16.7)	1(3.0)	10(30.3)	
Slight deterioration	3(4.5)	1(3.0)	2(6.1)	
Marked deterioration	0(0.0)	0(0.0)	0(0.0)	

Table 2. Effect of oxygen therapy on clinical parameters in HFNC and COT groups

	HFNC group (n = 33)			COT group (n = 33)			Between groups
Parameter	T0	T60	Differences* (95% CI)	T0	T60	Differences* (95% CI)	Differences** (95% CI)
Arterial PH	7.33	7.33	0.005 (-0.03 to 0.02)	7.31	7.27	-0.04 (-0.01 to 0.09)	0.03 (-0.02 to 009)
$PaCO_2$	48.8	44.1	4.7(1.9 to 7.5)	41.4	49.5	8.1(3.0 to 13.2)	12.8(7.0 to 18.6)
HCO_3	25.4	24.6	0.8(-0.6 to 2.3)	33.0	35.3	2.3(-3.3 to 8.0)	3.2(-2.7 to 9.1)
Pulse Oximetry	82.2	90.5	8.3(6.7 to 9.9)	82.8	82.3	0.5(-0.9 to 1.8)	8.8(6.8 to 10.9)
Respiratory rate	24.2	21.2	3.0(1.4 to 4.5)	24.6	24.4	0.2(-1.0 to 1.4)	2.8(0.8 to 4.6)
Heart rate	86.3	84.1	2.2(0.4 to 4.1)	88.2	87.8	0.4(-0.8 to 1.5)	1.8(0.3 to 4.1)
Systolic blood pressure	129.9	128.6	1.3(-1.9 to 4.4)	131.5	130.0	1.5(-0.8 to 1.8)	0.2(-4.4 to 4.9)
Diastolic blood pressure	80.8	77.8	3.0(-0.1 to 6.2)	81.1	80.8	0.3(-2.2 to 2.6)	2.7(-1.1 to 6.7)

* The differences in parameters by 60 minutes within each group

** The differences for the contrast in the differences between the HFNC and COT groups

Data are presented as mean. Differences are reported as mean differences (95% CI).

ICU admission was required in 51.5% of patients in the COT group versus 15.2% in the HFNC group (P = 0.002). There were no serious adverse events reported in either study group. Finally, patients in the HFNC group had a higher patient dyspnea improvement than those in the COT group (P=0.002). In the HFNC group, 93.9% of patients felt an improvement in their dyspnea after 60 min, but it was 63.7% in the COT group.

DISCUSSION

The present study showed that the use of HFNC compared with COT in ED patients presenting with acute respiratory failure was associated with a reduction in intubation and ICU admission rate and an improvement in the patient's dyspnea and comfort.

Several studies demonstrated that HFNC reduced the need for intubation in patients with ARF. A meta-analysis by Rochwerg et al. (10) which included 7 trials (n=1647) reported that HFNC therapy significantly reduced the intubation rate compared to COT. In addition, two meta-analyses by Monro– Somerville et al. (11) and Bocchile et al. (12) revealed the same result. In contrast, Macé et al. (1) and Tinelli et al. (2) did not observe any difference in terms of intubation rate in the HFNC group compared to COT. The discrepancy in the results may be due to differences in the cause of the ARF, the severity of the patients, and the number of subjects in the study.

In a large trial, Frat et al. (13) assessed the need for intubation in 310 subjects with ARF and demonstrated no difference in the intubation rate among those treated with HFNC, COT, or NIV. However, the intubation rate significantly was lower in HFNC versus COT and NIV in the subgroup with the most severe hypoxemia at baseline (PaO_2/FiO_2 ratio ≤200). While HFNC is generally indicated for patients with mild to moderate hypoxia, there is no clear association between the effect of HFNC and the cause of ARF. The increase in invasive treatment is more likely to occur in patients with acute respiratory stress syndrome (14).

In the present study, the ICU admission rate was lower in the HFNC group. However, previous studies did not show any difference in the need for ICU admissions (1,6, 15). This may be a reflection of the different policies of inpatient care in different hospitals. In some hospitals, all patients receiving HFNC were required to be admitted to a high-dependency unit due to staffing restrictions on the ward. On the other hand, few studies have been done in the ED.

The current study showed that patients in the HFNC group had better dyspnea improvement and satisfaction than those in the COT group. This result was similar to most previous studies (1,5,6,15). Of course, the scoring systems in the studies were different, but the results were consistent. Vargas et al. in twelve subjects admitted to the ICU for ARF demonstrated no significant improvement in shortness of breath with HFNC versus COT (16).

The present study demonstrated that HFNC therapy, compared with COT, significantly improved oxygen saturation, decreased $PaCO_2$, and reduced the respiratory rate and heart rate. Similarly, previous studies reported that HFNC, compared with COT, improved SpO_2 without affecting $PaCO_2$, and reduced the RR and clinical signs of respiratory distress (1,14, 17-19). HFNC can produce about 2–4 cm H_2O positive end-expiratory pressure; therefore, eliminating some airway dead space, decreasing $PaCO_2$ level, and improving SpO_2 (6). In the present study, the most common cause of ARF was in COPD patients and their PCO_2 indeed increased after COT therapy. However, they showed dramatic decreases in PCO_2 after HFNC therapy, which is in line with the results of previous studies that were conducted in stable COPD patients (20,21).

Rittayamai et al. showed that HFNC therapy compared with the COT significantly reduced RR, and HR at the end of the study. But, no significant differences in SpO_2 were found between the two groups (5). Bell et al. showed a higher proportion of patients with decreased RR after HNFC therapy (67%) than COT therapy (38%) (15).

Limitations

There were some limitations in the current study. First, it was a single-center study. Second, the study had a relatively small number of participants. Third, the inability to blind the treating team to the devices used may have biased the outcome measures. Finally, we did not measure hospital and ICU length and mortality.

CONCLUSION

HFNC was demonstrated to reduce the need for intubation and ICU admission in subjects presenting to the emergency department with acute respiratory failure compared with COT. In addition, HFNC was associated with a greater reduction in RR and improvement in SpO_2 compared with COT. Therefore, this device should be considered as first-line therapy in patients requiring oxygen therapy in the emergency department.

Funding

This study was funded by Isfahan University of Medical Sciences.

Conflict of Interests

The authors declare no conflict of interest.

REFERENCES

1. 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(11):2091-6.
2. Tinelli V, Cabrini L, Fominskiy E, Franchini S, Ferrante L, Ball L, et al. High Flow Nasal Cannula Oxygen vs. Conventional Oxygen Therapy and Noninvasive Ventilation in Emergency Department Patients: A Systematic Review and Meta-Analysis. ***J Emerg Med*** 2019;57(3):322-8.
3. Vincent JL, Sakr Y, Ranieri VM. Epidemiology and outcome of acute respiratory failure in intensive care unit patients. ***Crit Care Med*** 2003;31(4 Suppl):S296-9.
4. Stefan MS, Shieh MS, Pekow PS, Rothberg MB, Steingrub JS, Lagu T, et al. Epidemiology and outcomes of acute respiratory failure in the United States, 2001 to 2009: a national survey. ***J Hosp Med*** 2013;8(2):76-82.
5. 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(10):1377-82.
6. Huang CC, Lan HM, Li CJ, Lee TH, Chen WL, Lei WY, et al. Use High-Flow Nasal Cannula for Acute Respiratory Failure Patients in the Emergency Department: A Meta-Analysis Study. ***Emerg Med Int*** 2019;2019:2130935.
7. O'Driscoll BR, Howard LS, Davison AG; British Thoracic Society. Emergency oxygen use in adult patients: concise guidance. ***Clin Med (Lond)*** 2011;11(4):372-5.
8. Lenglet H, Sztrymf B, Leroy C, Brun P, Dreyfuss D, Ricard JD. Humidified high flow nasal oxygen during respiratory failure in the emergency department: feasibility and efficacy. ***Respir Care*** 2012;57(11):1873-8.
9. Lee CC, Mankodi D, Shaharyar S, Ravindranathan S, Danckers M, Herscovici P, et al. High flow nasal cannula versus conventional oxygen therapy and non-invasive ventilation in adults with acute hypoxemic respiratory failure: A systematic review. ***Respir Med*** 2016;121:100-8.
10. 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(5):563-72.
11. Monro-Somerville T, Sim M, Ruddy J, Vilas M, Gillies MA. The Effect of High-Flow Nasal Cannula Oxygen Therapy on Mortality and Intubation Rate in Acute Respiratory Failure: A Systematic Review and Meta-Analysis. ***Crit Care Med*** 2017;45(4):e449-56.
12. Bocchile RLR, Cazati DC, Timenetsky KT, Serpa Neto A. The effects of high-flow nasal cannula on intubation and re-intubation in critically ill patients: a systematic review, meta-analysis and trial sequential analysis. ***Rev Bras Ter Intensiva*** 2018;30(4):487-95.

13. 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(23):2185-96.
14. Spicuzza L, Schisano M. High-flow nasal cannula oxygen therapy as an emerging option for respiratory failure: the present and the future. ***Ther Adv Chronic Dis*** 2020;11:2040622320920106.
15. 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(6):537-41.
16. 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(10):1369-76.
17. Nishimura M. High-flow nasal cannula oxygen therapy in adults. ***J Intensive Care*** 2015;3(1):15.
18. Roca O, Riera J, Torres F, Masclans JR. High-flow oxygen therapy in acute respiratory failure. ***Respir Care*** 2010;55(4):408-13.
19. Sztrymf B, Messika J, Mayot T, Lenglet H, Dreyfuss D, Ricard JD. Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: a prospective observational study. ***J Crit Care*** 2012;27(3): 324.e9-13.
20. Bräunlich J, Seyfarth HJ, Wirtz H. Nasal High-flow versus non-invasive ventilation in stable hypercapnic COPD: a preliminary report. ***Multidiscip Respir Med*** 2015;10(1):27.
21. Kim ES, Lee H, Kim SJ, Park J, Lee YJ, Park JS, et al. Effectiveness of high-flow nasal cannula oxygen therapy for acute respiratory failure with hypercapnia. ***J Thorac Dis*** 2018;10(2):882-8.