International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)

Journal Home page: www.iscientific.org/Journal.html

Predictors of outcome of high flow nasal cannula in acute type 2 respiratory failure

Nasser Abdulnaby[1], Hamed Abdel Hafiz[1], Waleed Arafat[2], Samar Farrag[1], Gihan Abo Elwafa[1]*

[1]*Department of Chest diseases, Faculty of medicine, Cairo university, Cairo, Egypt*

[2]*Department of Chest diseases, Faculty of medicine, Beni-Suef university, Beni-Suef, Egypt*

Abstract

Despite being the gold standard for treatment of acute hypercapnic respiratory failure and its wide potential for application, non-invasive ventilation (NIV) use can be limited due to patient intolerance. High-flow nasal cannula (HFNC) is a newly-introduced oxygen delivery device extensively studied in hypoxemic respiratory failure and is of increasing interest as an alternative to NIV in hypercapnic respiratory failure. Our aim was to assess efficacy and safety of HFNC as an alternative to NIV in management of acute hypercapnic respiratory failure. patients with acute hypercapnic respiratory failure who received HFNC or NIV were enrolled. Clinical data, arterial blood gases analyses and laboratory investigations were collected. There was no significant difference between the HFNC and NIV groups in the terms of success rate (60.9% versus 69.6%) and length of ICU stay (11.35 ± 5.61 days versus 11.43 ± 6.67 days). However, there was statistically significant difference between the 2 groups in the terms of ICU mortality (17.4% for the HFNC group, versus 52.2% for the NIV group). HFNC can be a good alternative to NIV in management of acute hypercapnic respiratory failure.

Keywords: Respiratory failure, Non-invasive ventilation, High-flow nasal cannula.

Full length article **Corresponding Author*, e-mail: samar.mohamed1691@gmail.com

1. Introduction

Acute respiratory failure remains one of the major indications for intensive care unit (ICU) admission and it is a great challenge for physicians. It has a significant mortality and morbidity rates, increased risk of mechanical ventilation and high cost of treatment [1]. Acute type two respiratory failure is characterized by arterial hypercapnia ($PaCO_2$ > 6 kPa or >45 mmHg). Treatment aims at reversing the underlying disease processes along with controlled oxygen therapy, to decrease the work of breathing and alleviate hypoxia and hypercapnia. Patients often require ventilatory support and the current guidelines recommend the initial use of non-invasive ventilation (NIV) [2]. However, NIV exhibit several disadvantages, that can easily lead to its failure with subsequent endotracheal intubation, including facial compression, affection of patient communication, eating and sleep, leaks and asynchrony [3]. High-flow nasal cannula (HFNC) is an oxygen delivery device which employs high inspiratory flows of up to 60 liters/minute through a nasal cannula to deliver up to 100% fraction of inspired oxygen (FiO_2). HFNC was found to be superior to conventional oxygen therapy and equivalent to NIV in acute hypoxemic respiratory failure [4]. European respiratory society guidelines in 2022 stated that its role in acute hypercapnic respiratory failure is not yet well established and that more evidence is required before HFNC could be non-inferior to NIV [5].

2. Materials and Methods

This study was conducted in the respiratory intensive care unit, Chest Department, faculty of medicine, Cairo University in the period from October 2021 to October 2022. The study has been approved by the research ethics committee of faculty of medicine, Cairo University (No:MD-100-2021) and was conducted in accordance with the Helsinki Declaration. Written informed consent was obtained from all patients. We included patients with acute hypercapnic respiratory failure with age >18 years treated with either NIV (Draeger Evita V 300, Lubek, Germany) or HFNC (AIRVO2- Fisher HFNC device, Fisher & Paykel Healthcare Ltd., Auckland, New Zealand). Our study aimed to describe the outcome of patients with acute type two respiratory failure who received HFNC therapy versus those who received NIV.

The primary outcomes were success of HFNC, intubation rate and ICU mortality. Secondary outcomes included improvement in physiological and arterial blood gases (ABG) analyses parameters.

2.1. Data collection

History taking including comorbidities and need for long term oxygen therapy (LTOT), physical examination including assessment of vital signs and conscious level on admission and after 1, 4, and 6 hours of treatment. ABG analysis on admission, 1, 4, 6 hours after initiation of NIV or HFNC, total leucocytic count (TLC), C-reactive protein (CRP), kidney and liver function tests and serum electrolytes (Na, K) were recorded. Acute physiology and chronic health evaluation II (APACHE II) score, Charlson comorbidity index were calculated for all patients and ROX index was calculated for those treated with HFNC. HFNC failure was defined as any of the following: intolerance to treatment, persistent or worsening dyspnea, persistent abdominal paradox, respiratory rate $\geq$ 35 breath/min, systolic blood pressure < 90mmHg, increase in PCO_2 by > 10mmHg, decrease in pH by > 0.08 [6]. NIV failure was defined as any of the following: deterioration in patient's condition, failure to improve or deterioration in ABG parameters, development of new symptoms or complications, intolerance or failure of coordination with the ventilator, failure to alleviate symptoms, deteriorating conscious level [7].

2.2. Statistical analysis

Data were statistically described in terms of mean ± standard deviation (SD), or frequencies (number of cases) and percentages when appropriate. Numerical data were tested for the normal assumption using Kolmogorov Smirnov test. Comparison of numerical variables between the study groups was done using Student t test for independent samples in comparing normally distributed data and Mann Whitney U test for independent samples for comparing not-normal data. Within group comparison of numerical variables was done using paired t test in comparing normally distributed data and Wilcoxon signed rank test for paired (matched) samples when data are not normally distributed. For comparing categorical data, Chi-square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Two-sided p values less than 0.05 was considered statistically significant. IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows was used for all statistical analyses.

3. Results and Discussion

The study included 46 patients, 23 patients treated with HFNC and 23 treated with NIV. No device-related complications were recorded in both groups. HFNC was successful in 14 patients (60.9%) and NIV was successful in 16 patients (69.6%). Regarding the intubation rate, 1 patient only (4.35%) required intubation within the HFNC group, and 4 patients (17.4%) in the NIV group required intubation. Within the HFNC group, 4 patients (17.4%) died in the ICU, while 12 patients (52.2%) died within the NIV group. The mean duration of ICU stay was 11.35 ± 5.61 days for HFNC group and 11.43 ± 6.67 days for NIV group. The diagnoses within HFNC group were chronic obstructive pulmonary disease (COPD) (43.5%), obesity hypoventilation syndrome (OHS) (21.7%), interstitial lung diseases (ILD) (17.4%), bronchiectasis (13%), and 4.3% were undiagnosed. Among the NIV group, the diagnoses were COPD (69.6%), ILD (13%), bronchiectasis (8.7%), and kyphoscoliosis (8.7%). Table 1 summarizes the demographics and clinical scores of the study population. Fifteen patients in HFNC group (65.2%) had comorbidities, in the form of systemic hypertension (47.8%), diabetes mellitus (39.1%), ischemic heart disease (21.7%), hypothyroidism (4.35%), and malignancy (4.35%). Among NIV group, 12 patients (52.2%) had comorbidities, in the form of systemic hypertension (52.2%), diabetes mellitus (34.8%), ischaemic heart disease (17.4%), and arrhythmias (8.7%). Table 2 summarizes heart rate, respiratory rate, ABG analysis and laboratory investigations results of the study population. Table 3 compares pH, PCO_2, heart rate and respiratory rate on admission and after 1 hour of therapy. Table 4 and 5 summarizes factors that were found to be predictors of success and mortality within the HFNC group, respectively. Some of the mechanisms of action of HFNC that can help in the treatment of acute hypercapnic respiratory failure include a carbon dioxide washout effect of the upper airway dead space, permitting a more effective alveolar ventilation. HFNC also improves gas exchange and oxygenation in a flow dependent manner [8]. The used high flow rates produce an expiratory pharyngeal pressure (CPAP effect) which can counterbalance the intrinsic positive end-expiratory pressure and reduces airway inspiratory resistance present in these patients thus, decreasing the work of breathing [6]. Also, heated and humidified air help clearance of secretion and may reduce bronchoconstriction [9]. In our study, there was no statistically significant difference between HFNC and NIV groups in terms of success, intubation rate and ICU stay, however, HFNC group had significantly lower mortality rate. These agreed with the previous studies [6,8-12]. After 1 hour of treatment, HFNC caused statistically significant reduction in respiratory rate and increase in pH, also it reduced heart rate and PCO_2 although this was statistically in significant. Papachatzakis et al., stated that HFNC oxygen therapy led to a significant decrease of PCO_2 levels, and Golmohamad et al., found that post-treatment PCO_2 and pH significantly improved from baseline [9,13]. Yuste et al., reported a statistically significant increase in pH and a non-statistically significant decrease in respiratory rate and PCO_2 after 1 hour of treatment, while Espiney et al., reported reduction in heart rate and PCO_2, and no change in respiratory rate or pH after 1 hour of treatment [6,11]. As far as we know, this is the first study to assess the predictors of outcome of HFNC in hypercapnic respiratory failure. In this study, history of LTOT, pH and PCO_2 after 1 hour of therapy were significantly different between patients who succeeded or failed HFNC therapy. Also, BMI, APACHE II score after 24 hours, ROX index after 1 hour, heart rate after 1 hour and serum sodium were found to be significantly different between patients who survived or died after HFNC therapy which may give those factors an ability to predict outcome and mortality with HFNC therapy, respectively. Although the present results represent the data of a small number of patients but it may be an addition to the accumulating knowledge needed to recommend the use of HFNC in acute hypercapnic respiratory failure.

Table 1: Demographics and clinical scores of study population.

	HFNC		NIV		p value
	Count	%	Count	%	
Male sex	8	34.8	13	56.5	0.139
Comorbidities	15	65.2	12	52.2	0.369
History of LTOT	6	26.1	5	21.7	0.730
	Mean ± SD		Mean ± SD		
Age (years)	60.17 ± 9.47		62.09 ± 9.71		0.567
Body mass index (kg/m^2)	29.9 ± 6.79		28.19 ± 8.49		0.382
APACHE II score on admission	12.48 ± 4.19		11.83 ± 3.99		0.247
APACHE II score after 24 hours	9.57 ± 3.23		9.57 ± 4.32		0.565
Charlson comorbidity index	3.04 ± 1.61		3.3 ± 2.03		0.722
ROX index on admission	10.59 ± 5.32		-----		---
ROX index after 1 hour	9.97 ±3.79		-----		---

Table 2: Heart rate, respiratory rate, ABG analysis and laboratory investigations results of the study population.

	HFNC	NIV	p value
	Mean ± SD	Mean ± SD	
pH on admission	7.30 ± 0.03	7.29 ± 0.04	0.420
pH after 1 hour	7.33 ± 0.08	7.35 ± 0.08	0.428
pCO_2 on admission (mmHg)	65.61 ± 14.58	80.70 ± 16.54	**0.002**
pCO_2 after 1 hour (mmHg)	61.3 ± 14.79	68.13 ± 18.49	0.153
Heart rate on admission (beat/minute)	102.7 ± 18.09	102.04 ± 17.02	0.939
Heart rate after 1 hour (beat/minute)	100.87 ± 27.63	102.04 ± 16.33	0.531
Respiratory rate on admission (cycle/minute)	27.52 ± 6.16	28.96 ± 6.51	0.355
Respiratory rate after 1 hour (cycle/minute)	26.04 ± 5.54	25.43 ± 4.47	0.572
Hemoglobin (g/dl)	12.57 ± 2.1	12.09 ± 2.5	0.429
Total leucocytic count (x10^3/cm^3)	13.05 ± 8.06	15.19 ± 10.56	0.160
Platelet count (x10^3/cm^3)	293.57 ± 112.1	308.48 ± 96.41	0.637
Serum sodium (mmol/liter)	134.74 ± 5.58	137.96 ± 4.59	0.061
Serum potassium (mmol/liter)	4.84 ± 0.72	4.44 ± 0.58	0.053
Serum urea (mg/dl)	70.5 ± 44.12	46.2 ± 25.98	0.066
Serum creatinine (mg/dl)	1.22 ± 0.59	0.86 ± 0.43	**0.023**
Serum albumin (g/dl)	3.31 ± 0.47	3.26 ± 0.6	0.877
CRP (mg/liter)	59.22 ± 73.02	91.64 ± 82.47	0.059
Random blood glucose (mg/dl)	180.35 ± 99.9	182.13 ± 68.91	0.317

Table 3: Comparison of some parameters on admission and after 1 hour.

HFNC			
	on admission	**after 1 hour**	**p value**
Heart rate (beat/minute)	102.7 ± 18.09	100.87 ± 27.63	0.294
Respiratory rate (cycle/minute)	27.52 ± 6.16	26.04 ± 5.54	**0.029**
pH	7.30 ± 0.03	7.33 ± 0.08	**0.035**
PCO_2 (mmHg)	65.61 ± 14.58	61.3 ± 14.79	0.051
NIV			
Heart rate (beat/minute)	102.04 ± 17.02	102.04 ± 16.33	0.958
Respiratory rate (cycle/minute)	28.96 ± 6.51	25.43 ± 4.47	**0.000**
pH	7.29 ± 0.04	7.35 ± 0.08	**0.001**
PCO_2 (mmHg)	80.70 ± 16.54	68.13 ± 18.49	**0.001**

Table 4: Predictors of success of HFNC.

	Success		**Failure**		**p value**
	Count	**%**	**Count**	**%**	
History of LTOT	6	42.9	0	0	**0.022**
	Mean ± SD		Mean ± SD		
pH after 1 hour	7.38 ± 0.04		7.25 ± 0.07		**0.000**
pCO_2 after 1 hour (mmHg)	54.64 ± 9.54		71.67 ± 15.97		**0.009**

Table 5: Predictors of mortality in HFNC.

	Died	Survived	p value
	Mean ± SD	Mean ± SD	
BMI (kg/m^2)	23.25 ± 5.32	31.34 ± 6.3	**0.037**
APACHE II score after 24 hours	14 ± 2.6	8.63 ± 2.5	**0.005**
ROX index after 1 hour	6.5 ± 3	10.71 ± 3.6	**0.042**
Heart rate after 1 hour (beat/minute)	122.25 ± 13.79	96.37 ±27.9	**0.015**
Serum sodium (mmol/liter)	127.75 ± 3.40	136.21 ± 4.79	**0.006**

4. Conclusions

From our study we concluded that HFNC could be used in patients with mild to moderate acute hypercapnic respiratory failure as an alternative to NIV, followed-up by trained ICU staff who can accurately assess treatment response and perform immediate intubation when needed.

Acknowledgement
None.

Disclosure of interest
Authors report no conflict of interest.

Financial support
None.

References

[1] J. L. Vincent, H. S. Suri, G. Li, & O. Gajic. (2008). Epidemiology of acute respiratory failure and mechanical ventilation. In Yearbook of intensive care and emergency medicine (pp. 193-202). Springer Berlin Heidelberg.

[2] A. A. Alnajada, B. Blackwood, A. Mobrad, A. Akhtar, I. Pavlov, & M. Shyamsundar. (2021). High flow nasal oxygen for acute type two respiratory failure: a systematic review. F1000Research. 10: 482.

[3] Z. Xu, L. Zhu, J. Zhan, & L. Liu. (2021). The efficacy and safety of high-flow nasal cannula therapy in patients with COPD and type II respiratory failure: a meta-analysis and systematic review. European journal of medical research. 26 (1): 122.

[4] Y. Huang, W. Lei, W. Zhang, & J. A. Huang. (2020). High-Flow Nasal Cannula in Hypercapnic Respiratory Failure: A Systematic Review and Meta-Analysis. Canadian respiratory journal. 7406457.

[5] S. Oczkowski, B. Ergan, L. Bos, M. Chatwin, M. Ferrer, C. Gregoretti, L. Heunks, J. P. Frat, F. Longhini, S. Nava, P. Navalesi, A. Ozsancak Uğurlu, L. Pisani, T. Renda, A. W. Thille, J. C. Winck, W. Windisch, T. Tonia, J. Boyd, G. Sotgiu, …, & R. Scala. (2022). ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. The European respiratory journal. 59 (4): 2101574.

[6] M. E. Yuste, O. Moreno, S. Narbona, F. Acosta, L. Peñas, & M. Colmenero. (2019). Efficacy and safety of high-flow nasal cannula oxygen therapy in moderate acute hypercapnic respiratory failure. Eficácia e segurança da oxigenoterapia com cânula nasal de alto fluxo na insuficiência respiratória hipercápnica moderada aguda. Revista Brasileira de terapia intensive. 31 (2): 156–163.

[7] A. C. Davidson, S. Banham, M. Elliott, D. Kennedy, C. Gelder, A. Glossop, ... & L. Thomas. (2016). BTS/ICS guideline for the ventilatory management of acute hypercapnic respiratory failure in adults. Thorax. 71 (Suppl 2): ii1-ii35.

[8] J. Sun, Y. Li, B. Ling, Q. Zhu, Y. Hu, D. Tan, P. Geng, & J. Xu. (2019). High flow nasal cannula oxygen therapy versus non-invasive ventilation for chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: an observational cohort study. International journal of chronic obstructive pulmonary disease. 14: 1229–1237.

[9] A. Golmohamad, R. Johnston, K. Hay, & G. Tay. (2022). Safety and efficacy of high-flow nasal cannula therapy in acute hypercapnic respiratory failure: a retrospective audit. Internal medicine journal. 52 (2): 259–264.

[10] M. K. Lee, J. Choi, B. Park, B. Kim, S. J. Lee, S. H. Kim, S. J. Yong, E. H. Choi, & W. Y. Lee. (2018). High flow nasal cannulae oxygen therapy in acute-moderate hypercapnic respiratory failure. The clinical respiratory journal. 12 (6): 2046–2056.

[11] R. Espiney, J. Jablonski, & M. Brys. (2019). Humidified High Flow Nasal Cannula Algorithm for Primary Therapy in Hypercapnic Respiratory Failure. Global Journal of Anesthesia & Pain Medicine. 1: 86-91.

[12] A. Cortegiani, F. Longhini, F. Madotto, P. Groff, R. Scala, C. Crimi, ... & HF-AECOPD study investigators Lorenzo Ball Tiziana Bove Raffaele Campisi Paola Chirco Maria Stella Dionisi Mariachiara Ippolito Riccardo Fantini Luca Guidelli Uberto Maccari Luca Tabbì Maria Rita Taliani. (2020). High flow nasal therapy versus noninvasive ventilation as initial ventilatory strategy in COPD exacerbation: a multicenter non-inferiority randomized trial. Critical Care. 24: 1-13.

[13] Y. Papachatzakis, P. T. Nikolaidis, S. Kontogiannis, & G. Trakada. (2020). High-Flow Oxygen through Nasal Cannula vs. Non-Invasive Ventilation in Hypercapnic Respiratory Failure: A Randomized Clinical Trial. International journal of environmental research and public health. 17 (16): 5994.