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High Flow Nasal Cannula in Preventing Reintubation in Extubated Patients with Treated Type I Respiratory Failure

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Abstract

Background: Respiratory failure (RF) is a syndrome caused by a multitude of pathological states; therefore, the epidemiology of this disease process is difficult to ascertain. In 2017, in the United States of America, however, the incidence of respiratory failure was found to be 1,275 cases per 100,000 adults. The case definition used in this study included all diagnosis codes that included respiratory failure as a component. The epidemiology of respiratory failure is dependent mainly on the cause leading to the failure. Below, some common causes of respiratory failure and the relevant trends are listed.

Aim of Study: Evaluation of the efficacy of high flow nasal cannula (HFNC) in reducing the risk of reintubation following extubation of patients with treated type I respiratory failure.

Subjects and Methods: This study was a prospective study conducted on 128 extubated patients with type I respiratory failure to compare the results from using HFNC versus Conventional oxygen mask. The study period from February 2024 to Augusts 2024.

Results: The HR for the HFNC group compared to the conventional therapy group is 0.26 (95% CI: 0.12, 0.60), with a significant difference between the two groups (p=0.002). Our results suggested that patients in the HFNC group had a substantial benefit of increasing the time to reintubation compared to patients in the conventional therapy group.

Conclusion: Our study findings contribute valuable insights into the ongoing evaluation of HFNC therapy. While HFNC did not demonstrate significant advantages in terms of weaning time or ICU length of stay, it did show a noteworthy benefit of increasing time to reintubation. Future studies should aim to explore these variables and refine HFNC protocols to optimize patient outcomes across diverse clinical settings.

Key Words: High Flow Nasal Cannula – Reintubation – Extubation – Type I respiratory failure.

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Introduction

MECHANICAL ventilation is associated with significant complications that are time-dependent in nature, with a longer duration of intubation resulting in a higher incidence of complications, such as ventilator-associated pneumonia (VAP) and increased mortality.

High-flow nasal cannula (HFNC) oxygen therapy supplies heated and humidified oxygen via a nasal cannula device; high flow rates generate low-level positive pressure when the mouth is closed, resulting in a decrease in carbon dioxide level within the anatomic dead space.

As a result, HFNC is believed to improve patient comfort, enhance the expectoration of secretions, and decrease the work of breathing.

Moreover, HFNC can supply highly concentrated oxygen (up to 100%), which is not possible for conventional oxygen delivery systems. Several studies have reported physiological and clinical benefits associated with HFNC in respiratory care **[1]**.

Liberation and extubation are important elements in care of patients supported by mechanical ventilation. The success rate of extubation is related to the duration of stay within an intensive care unit (ICU). The mortality rates are associated with the underlying condition **[2]**.

Following planned extubation, selection of oxygen delivery modality is at the discretion of the attending physician.

As previous studies have shown a positive effect of HFNC in postextubation patients **[3]**. We hypothesized that using HFNC following extubation will reduce incidence of reintubation.

Aim of the work:

Evaluation of the efficacy of high flow nasal cannula (HFNC) in reducing the risk of reintubation following extubation of patients with treated type I respiratory failure.

Patients and Methods

This prospective randomized controlled trial, open-labeled, was conducted at Ain Shams University Hospitals over a 6-month period following protocol approval. The study population comprised extubated patients aged 30-70 years with treated type I respiratory failure using a high flow nasal cannula. Inclusion criteria were admission to the ICU and extubation after intubation due to type I respiratory failure caused by pulmonary edema, pneumonia, acute respiratory distress syndrome, or idiopathic pulmonary fibrosis. Exclusion criteria included terminally ill and comatose patients, disturbed level of consciousness, post cardiac arrest, $PaCO_2$ >50mmHg, and a history of type II respiratory failure.

Sampling method: Simple random computer-generated sampling (SRS).

Sample size: Maggiore and his colleagues in 2014 reported rate of reintubation of 21.2% in the control group and 3.8% in NHF group. A sample size of at least 64 cases per group – totaling 128 cases – achieves a power of 80% to detect a difference in reintubation rate of 17.4% using unpooled z-test between two independent proportions with level of significance of 0.05. The sample is inflated by 20% to compensate for the dropouts.

Ethical considerations: Ethical approval was obtained from medical ethical committee of Faculty of Medicine, Ain Shams University, as well as informed written consent from the patients.

Study tools: High velocity nasal cannula for adult (VAPOTHERM Hi-VNI Technology) and conventional oxygen mask.

Patients and methods: The patients included where those who met the weaning criteria according to the following protocol.

Weaning protocol: Patients fulfilling the criteria for extubation underwent a SBT following the local protocols. The SBT ranged from 30 to 120min and was performed with 5-cmH_2O continuous positive airway pressure, 7-cmH_2O pressure support, or T-tube. Criteria for SBT failure were agitation, anxiety, depressed mental status, diaphoresis, cyanosis, evidence of increasing respiratory effort, working accessory muscle activity, facial signs of distress, dyspnea, PaO_2 ≤60mmHg or SpO_2 <90% on FiO_2>-0.5, $PaCO_2$ >50mmHg or >8mmHg increase, arterial pH <7.32 or >-0.07 decrease, respiratory rate >35 breaths min−1 or >-50% increase, heart rate >140 beats min^{-1} or >-20% increase, systolic arterial pressure >180mmHg or >-20% increase, systolic arterial pressure <90mmHg, or cardiac arrhythmia. Patients who failed the SBT were reconnected to the ventilator for an additional 24-h rest period before a new SBT. Patients who tolerated the SBT were directly extubated and randomized to receive either high-flow or conventional oxygen therapy for a fixed 24-h period. Randomization was performed via a computerized generated program and allocation was concealed through numbered opaque envelopes **[4]**, immediately after extubation.

The patients were randomized into two groups:

- Group A: Received oxygen treatment by "HFNC" High flow nasal cannula (adult).

The flow level of the HFNC began at 40L/min and was adjusted downward in 5- to 10-L/min every 1 hour targeting a stabilized alternating with Fio_2 .01.

- Group B: Received oxygen via conventional oxygen mask.

The flow rate of the conventional oxygen mask was set at 10L/min and the target was decreasing FGF by 4L/min every 1hr as long as SPO_2>92%.

The following data were obtained from all the cases according to our unit protocol:

Data collected from all cases according to our unit protocol included demographic characteristics such as age, gender, and name, as well as anthropometric data and comorbidities.

Simplified Acute Physiology Score (SAPS) II on ICU admission and diagnostic information were noted. The use of vasopressors (epinephrine, norepinephrine, phenylephrine, vasopressin, and dopamine) before extubation was recorded. Vital data (heart rate, blood pressure, temperature, respiratory rate, and oxygen saturation) were monitored at extubation and every 6 hours for 72 hours post-extubation. Arterial blood gases, including P/F ratio and $PaCO_2$, were also measured at extubation and every 6 hours for 72 hours thereafter. Additional data included SOFA score, rapid shallow breathing index (RSBI), and adverse events, such as the need to switch to a high flow nasal cannula (HFNC) **[5]**, or requiring non-invasive ventilation (NIV) or endotracheal intubation.

Each group results were collected and assessed for:

Primary outcome: The primary outcome variable was extubation failure within 72h.

Secondary outcome: Length of ICU stay, 28 days mortality and time till weaning from oxygen supplied.

The principal investigator held regular meeting with the research team to assess data of patient and adverse event. Any serious event was reported to the ethical committee within 24 hours.

Statistical analysis: The data were analyzed using R programming in R Studio. Categorical variables were compared using the Chi-square test, while continuous variables were compared using either student's *t*-test or the Mann-Whitney test, depending on the normality of variables.

Kaplan-Meier survival analyses were conducted to assess extubation failure. A multivariable logistic regression model was conducted to identify factors independently associated with postextubation respiratory failure. This model included age, gender, BMI, SAPS II score, APACHE II score, and other comorbidities associated with post-extubation respiratory failure. Statistical significance was determined at a *p*-value less than 0.05. This study was a prospective study conducted on 128 extubated patients with type I respiratory failure to compare the result from HFNC to Conventional oxygen mask.

Results

Demographic data:

Table (1): Demographic and clinical characteristics.

	HFNC (n =64)	Conventional (n =64)	*p*-value
Age, years	65.00±12.14+	63.42±11.74+	.0.46
Gender, Males	34 (53.1%)$	39 (60.9%)$	0.48
Gender, Females	30 (46.9%)$	25 (39.1%)$	0.48
BMI	27.6±7.77+	24.6±7.83+	0.09
SAPS II score on admission	40.3 (28.6-52)#	39.9 (24.4-55.4)#	0.88
APACHE II score on admission	23.2 (15.1-31.3)#	23.3 (13.5-33.1)#	0.96
SOFA score	2 (1-4)#	3 (2-4)#	0.64
RSBI	49 (29, 68)#	53 (32, 58)#	0.094
Length of mechanical ventilation (day)	9.88±4.30+	8.56±3.69+	0.06
The use of vasopressors	19 (29.6%)$	18 (28.12)$	0.09
Diabetic	43 (67.2%)$	41 (64.1%)$	0.85
Hypertensive	57 (89.1%)$	56 (87.5%)$	0.89
Liver disease	17 (26.6%)$	17 (26.6%)$	0.87
Renal disease	11 (17.2%)$	8 (12.5%)$	0.62
Hweart failure	26 (40.6%)$	24 (37.5%)$	0.86
Respiratory diseases	24 (37.5%)$	26 (40.6%)$	0.09
Coronary artery diseases	17 (26.6%)$	21 (32.8%)$	0.56
Replacement of the original oxygen system	6 (9.3%)$	7 (10.9%)$	0.07
Requiring NIV or endotracheal intubation	3 (4.6%)$	5 (7.8)$	0.06

HFNC = High-flow nasal cannula. Homogenous data were reported as mean (SD) using *t*-test (+), heterogenous data were reported as median [IQR] using Mann-Whitney test (#), and categorical data weres reported as number (%) using Chi-square test ($).

Our study showed that all demographic and clinical characteristics were generally comparable between patients receiving HFNC therapy and those receiving conventional therapy. (Table 1).

Outcomes:

Table (2): Outcome variables in patients receiving HFNC and conventional therapy.

	Differences		*p*-value
	HFNC (n=64)	Conventional (n=64)	
Extubation failure (reintubation)	14 (21.9%)$	15 (23.4%)$	0.96
Time till weaning from oxygen supply (days)	2.50±1.15+	2.58±1.21+	0.66
Time to reintubation (hours)	22.07±4.61+	14.86±4.73+	0.005*
ICU length of stay (days)	7.73 (4.14-11.32)#	7.94 (4.22-11.66)#	0.83
28 days mortality	14 (21.9)$	16 (25.0%)$	0.83

HFNC = High-flow nasal cannula. Homogenous data were reported as mean (SD) using *t*-test (+), heterogenous data were reported as median [IQR] using Mann-Whitney test (#), and categorical data weres reported as number (%) using Chi-square test ($).

The comparison between patients receiving HFNC and conventional therapy revealed no statistically significant differences observed in the meantime till weaning from oxygen supply or in the ICU length of stay. However, a notable distinction emerged in the time to reintubation, with patients in the HFNC group exhibiting a significantly longer duration before reintubation compared to those in the conventional therapy group. These findings suggest that while HFNC therapy may not affect the duration of oxygen weaning or ICU length of stay, it could potentially delay the need for reintubation compared to conventional therapy. (Table 2).

The comparison of frequencies between patients receiving HFNC and conventional therapy revealed no significant differences in reintubation rates or 28-day mortality rates. Likewise, 28-day mortality rates in both groups were comparable. (Table 2).

Time to reintubation survival analysis:

Table (3): Time to reintubation survival analysis.

Characteristic (Patient group)	HR[1]	%95 CI1	*p*-value
Conv		Reference	
HFNC	0.26	0.12, 0.60	0.002*

HFNC = High-flow nasal cannula.
[1]HR = Hazard Ratio.
CI = Confidence Interval.
* = Significant results.

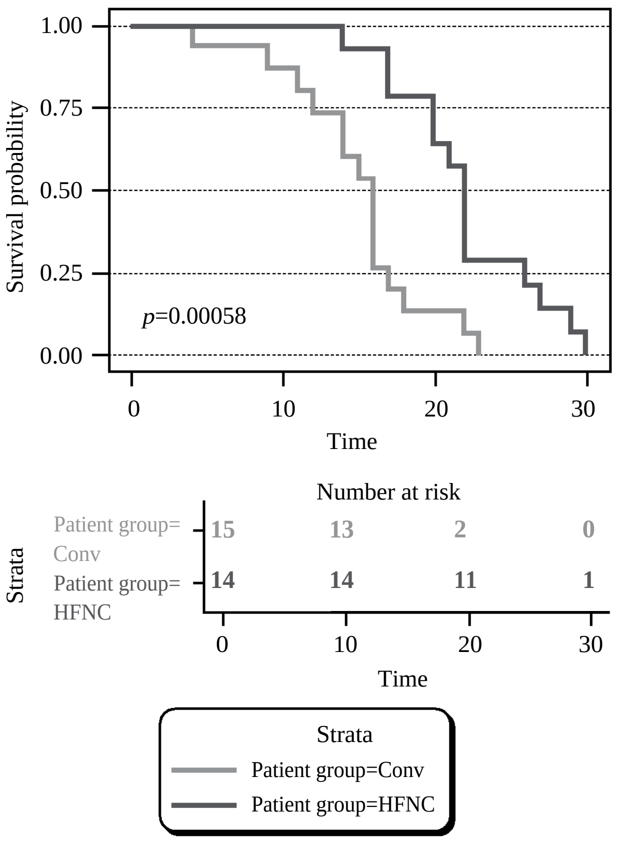

Fig. (1): Kaplan-Meier curves showing time to reintubation survival analysis.

Our results suggest that patients in the HFNC group have a substantially lower risk of experiencing reintubation compared to patients in the conventional therapy group. (Table 3, Fig. 1).

Regression:

Table (4): Logistic regression for post-extubation failure.

Characteristic	OR [1]	%95 CI [1]	*p*-value
Age, years	1.01	0.97, 1.04	0.8
Gender:			
Female		Reference	
Male	0.62	0.24, 1.53	0.3
BMI	0.99	0.94, 1.05	0.8
SAPS II score	1.01	0.98, 1.04	0.6
APACHE II score	0.95	0.90, 1.00	0.06
Length of mechanical ventilation, days	1.04	0.93, 1.17	0.5
SOFA score	1.05	0.95, 1.15	0.8
RSBI	0.58	0.28, 1.06	0.089
P/F ratio at extubation	1.15	0.54, 1.84	0.4
P/F ratio 72h post extubation	1.08	0.57, 1.94	0.3
PaCO2 at extubation	1.04	0.84, 1.48	0.6
PaCO2 72h post extubation	1.14	0.54, 1.79	0.2

Table (4): Count.

Characteristic	OR [1]	%95 CI [1]	*p*-value
Using of vasopressor:			
None		Reference	
Yes	1.8	0.86, 4.58	0.6
Diabetes:			
Not diabetic		Reference	
Diabetic	1.13	0.42, 2.96	0.8
Hypertension:			
Not hypertensive		Reference	
Hypertensive	1.70	0.40, 6.22	0.4
Liver disease:			
None		Reference	
Liver disease	0.30	0.11, 0.82	0.08
Renal disease:			
None		Reference	
Renal disease	0.75	0.20, 3.20	0.7
Heart failure:			
None		Reference	
Heart failure	0.87	0.34, 2.28	0.8
Coronary artery disease:			
None		Reference	
Coronary artery diseases	0.56	0.22, 1.46	0.2
Respiratory diseases:			
None		Reference	
Yes	0.72	0.34, 5.58	0.3
Replacement of the original oxygen system:			
None		Reference	
Yes	0.89	0.46, 4.38	0.07
Requiring NIV or endotracheal intubation:			
None		Reference	
Yes	0.73	0.56, 3.55	0.07

1 OR = Odds Ratio.
CI = Confidence Interval.
* = Significant results.

Discussion

Our study aimed to compare the effectiveness of High-Flow Nasal Cannula (HFNC) therapy against conventional oxygen therapy (COT) in terms of time to wean from oxygen supply, ICU length of stay, and time to reintubation. Our results showed that there were no statistically significant differences in the time until weaning from oxygen (2.50 days vs. 2.58 days) or ICU length of stay (7.73 days vs. 7.94 days) between the two groups. However, patients in the HFNC group experienced a significantly longer duration before reintubation.

Based on the above advantages, Parke et al. **[6]** and Xia et al. **[7]**, found that HFNC could improve comfort levels, increase oxygenation, and decrease the dyspnea score in adult patients. Nevertheless, there has been no clear consensus on treatment outcomes (such as intubation rate, escalated respiratory support rate, and mortality).

Compared to HFNC, noninvasive mechanical ventilation (NIV) can create a much higher gas flow rate and positive airway pressure but is uncomfortable and has many complications [8].

Our findings contribute to the ongoing debate regarding the relative efficacy of HFNC compared to COT. Our results are consistent with previous evidence conducted by Chen et al. [9], Hernández et al. [10], Granton et al. [11], Zhu et al. [12], Xu et al. [13], Huang et al. [14] and Hernández et al. [3]. Also, there is some evidence that diverges from our results, providing a nuanced view of HFNC's benefits, conducted by Ishihara et al. [15] and Zhu et al. [12].

In a study evaluating the effectiveness of HFNC in a mixed ICU population, Chen et al. [9] found that although HFNC was superior to COT improving respiratory function and coughing ability, they did not find a significant difference in 28-d mortality and ICU stay.

Moreover, Hernández et al. [10] aimed to determine whether NIV with active humidification is superior to HFNC in preventing reintubation in patients with ≥4 risk factors (very high risk for extubation failure). The study groups were comparable in demographic data to reduce the bias (including age, gender, SAPS II score, APACHE II score, length of mechanical ventilation, diabetes, hypertension, liver disease, and renal disease. They found that there were no significant differences in ICU and hospital length of stay, mortality rate, and severe adverse events between the studied groups.

Granton et al. [11] reported no significant differences in ICU or hospital length of stay between patients receiving high-flow nasal cannula (HFNC) and those on COT. The study found that HFNC significantly lowers reintubation rates compared to COT but does not show superior performance compared to noninvasive ventilation (NIV).

Zhu et al. [12] found that a high-flow nasal cannula (HFNC) significantly reduced postextubation respiratory failure and respiratory rates, and improved PaO_2 compared to COT.

However, there were no significant differences in ICU or hospital length of stay, mortality, or severe adverse events between the HFNC and COT groups. This indicates that while HFNC may offer benefits in respiratory management, it does not impact overall hospital outcomes or safety compared to COT.

A meta-analysis of seven randomized controlled trials conducted by Huang et al. [14] found that HFNC had comparable reintubation rates to both COT in overall patients. However, in critically ill patients, HFNC was associated with a lower reintubation rate compared to COT and improved patient tolerance and comfort.

Our results were supported by Hernández et al. [3] who aimed to test if high-flow conditioned oxygen therapy is non-inferior to NIV for preventing post-extubation respiratory failure and reintubation in patients at high risk of reintubation. The authors reported no significant deference between the studied groups regarding the meantime till weaning from oxygen supply and ICU length of stay.

In contrast to our results, Ishihara et al. [15] conducted a large observational study on the use of HFNC in patients with ARDS. Their results indicated that HFNC reduced mortality and ICU length of stay compared to COT. This contrasts with our findings suggesting that HFNC might be more effective in particular subgroups with fewer comorbidities and a lower mean APACHE II score of 18.

A meta-analysis by Xu et al. [13] reviewed multiple studies comparing HFNC with COT. The authors concluded that while HFNC did not consistently reduce time to reintubation and mortality outcomes, it did show a tendency to reduce reintubation and treatment failure rates. This metaanalysis contrasts our finding that HFNC benefits may be more pronounced in terms of delaying reintubation rather than affecting other outcome measures.

A study conducted by Zhu et al. [12] investigated HFNC versus COT in a broader range of ICU patients and found that HFNC demonstrated a higher success rate, better arterial oxygen levels, and lower respiratory rates. Additionally, HFNC was associated with less discomfort from interface displacement and airway dryness. This contrasts with our study's findings and can be explained by the smaller sample size and lower APACHE-II score in their population.

Reducing the reintubation rate was explained as HFNC after extubation could reduce the requirement for escalation of the respiratory support, improve oxygenation and respiratory parameters, reduce respiratory rate and work of breathing, provide patient comfort, and humidification with higher flow rates Song et al. [16] and Sztrymf et al. [17].

The variability in results across different studies underscores the need for further research to better understand the contexts and patient populations in which HFNC may offer the most benefit.

Our study limitations include a small number of patients, a shorter observed period for reintubation, and a lack of diversity of groups.

Conclusion:

Our study findings contribute valuable insights into the ongoing evaluation of HFNC therapy. While HFNC did not demonstrate significant advantages in terms of weaning time or ICU length of stay, it did show a noteworthy benefit of increasing the time to reintubation. Future studies should aim to explore these variables and refine HFNC protocols to optimize patient outcomes across diverse clinical settings.

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قنينة الأنف عالية التدفق فى منع إعادة التنبيب في المرضى الذين تم نزع أنبوبهم والذين عولجوا من النوع الأول من فشل الجهاز التنفسى

الخلفيـة: فشل الجهاز التنفسى (RF) هو متلازمة تنتج عن العديد من الحالات المرضية المختلفة، مما يجعل من الصعب تحديد الوبائيات الخاصة بهذه الحالة. ومع ذلك، فى عام ٢٠١٧ فى الولايات المتحدة الأمريكية، بلغ معدل حدوث فشل الجهاز التنفسى ١,٢٧٥ حالة لكل ١٠٠,٠٠٠ من البالغين. وشملت تعريفات الحالة المستخدمة فى هذه الدراسة جميع الأكواد التشخيصية التى تضمنت فشل الجهاز التنفسى كجزء منها. وتعتمد وبائيات فشل الجهاز التنفسى بشكل رئيسى على السبب المؤدى إلى الفشل. أدناه، تم سرد بعض الأسباب الشائعة لفشل الجهاز التنفسى والاتجاهات ذات الصلة.

الأهـداف: تقييم فعالية استخدام القنية الأنفية عالية التدفق (HFNC) فى تقليل خطر إعادة التنبيب بعد إزالة التنبيب لدى المرضى الذين تم علاجهم من فشل الجهاز التنفسى من النوع الأول.

الموضوعات والأساليب: كانت هذه الدرلسة دراسة مستقبلية شملت ١٢٨ مريضاً تم إزالة التنبيب لديهم بعد علاجهم من فشل الجهاز التنفسى من النوع الأول، حيث تمت مقارنة نتائج استخدام القنية الزنفية عالية التدفق (HFNC) مع قنا ع الأكسجين التقليدى.

النتائـج: بلغت نسبة المخاطرة (HR) لمجموعة القنية الأنفية عالية التدفق مقارنة بمجموعة لعلاج التقليدى ٠,٢٦ (فاصل الثقة ٩٥٪ : ١٢,٠–٦٠,٠)، مع وجود فرق ذو دلالة إحصائية بين المجموعتين. (*p*=0.002) أشارت نتائجنا إلى أن المرضى فى مجموعة القنية الأنفية عالية التدفق استفادوا بشكل كبير من زيادة الوقت قبل الحاجة إلى إعادة التنبيب مقارنة بالمرضى فى مجموعة العلاج التقليدى.

الاستنتاج: تساهم نتائج درستنا فى تقديم رؤى قيمة لتقييم استخدام القنية الأنفية عالية التدفق. فى حين أن القنية الأنفية عالية التدفق لم تُظهر فوائد ملحوظة فيما يتعلق بوقت الفطام أو مدة الإقامة فى وحدة العناية المركزة، إلا إنها أظهرت فائدة مهمة فى زيادة الوقت قبل الحاجة إلى إعادة التنبيب. ينبغى على الدراسات المستقبلية استكشاف هذه المتغيرات بشكل أكبر وتحسين بروتوكولات القنية الأنفية عالية التدفق لتحسين نتائج المرضى فى مختلف البيئات السريرية.