Comparison of the Effectiveness of High Flow Nasal Oxygen Cannula vs. Standard Non-Rebreather Oxygen Face Mask in Post-Extubation Intensive Care Unit Patients

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ABSTRACT: **Background:** Optimal oxygen supply is the cornerstone of the management of critically ill patients after extubation, especially in patients at high risk for extubation failure. In recent years, high flow oxygen system devices have offered an appropriate alternative to standard oxygen therapy devices such as conventional face masks and nasal prongs.

Objectives: To assess the clinical effects of high flow nasal cannula (HFNC) compared with standard oxygen face masks in Intensive Care Unit (ICU) patients after extubation.

Methods: We retrospectively analyzed 67 consecutive ventilated critical care patients in the ICU over a period of 1 year. The patients were allocated to two treatment groups: HFNC (34 patients, group 1) and non-rebreathing oxygen face mask (NRB) (33 patients, group 2). Vital respiratory and hemodynamic parameters were assessed prior to extubation and 6 hours after extubation. The primary clinical outcomes measured were improvement in oxygenation, ventilation-free days, re-intubation, ICU length of stay, and mortality.

Results: The two groups demonstrated similar hemodynamic patterns before and after extubation. The respiratory rate was slightly elevated in both groups after extubation with no differences observed between groups. There were no statistically significant clinical differences in $PaCO_2$. However, the use of HFNC resulted in improved PaO_2/FiO_2 post-extubation ($P < 0.05$). There were more ventilator-free days in the HFNC group ($P < 0.05$) and fewer patients required re-intubation (1 vs. 6). There were no differences in ICU length of stay or mortality.

Conclusion: This study demonstrated better oxygenation for patients treated with HFNC compared with NRB after extubation. HFNC may be more effective than standard oxygen supply devices for oxygenation in the post-extubation period.

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KEY WORDS: high flow nasal cannula (HFNC), non-rebreathing oxygen face mask (NRB), post-extubation complications

Extubation failure necessitating re-intubation is a common problem for ventilated critically ill patients. Many factors contribute to extubation failure, including muscle fatigue, hemodynamic instability, psychological discomfort, and an inability to protect the airway and clear secretions. Several oxygen devices and techniques have been used to decrease the rate of extubation failure and to support recently weaned patients [1,2], including non-invasive ventilation (NIV). In recent years, new techniques of oxygen supply have been introduced. High flow oxygen system devices provide an adequate alternative to conventional oxygen therapy such as face mask and nasal prongs in extubated patients. In the intensive care unit (ICU), high flow oxygen systems deliver warmed and humidified oxygen at a flow rate of 30–60 L/min. Most of these systems include high humidity face masks, high humidity tracheostomy collars, Venturi masks, large volume aerosol systems, and humidified high flow nasal cannula (HFNC). Two commonly used HFNC systems are the Optiflow™ Nasal Interfaces (Fisher & Paykel Healthcare, New Zealand) and the Vapotherm™ system (Vapotherm Inspiration Healthcare, United Kingdom) [3-5].

High flow oxygen system devices can also be used in the treatment of spontaneously breathing patients [7,8] with reduced oxygenation immediately after extubation, who are at risk of immediate re-intubation. HFNC has been shown to improve oxygenation post-extubation in the neonatal and pediatric populations [9-12]. Only a few small studies have been conducted in adult volunteers. It is unknown whether HFNC offers clear physiological advantages over a non-rebreathing (NRB) oxygen face mask (non-Venturi) in the immediate post-extubation period. In this study we compared the clinical effects of cardiovascular and respiratory systems and primary outcome variables in patients treated with HFNC compared with NRB following extubation in an adult ICU.

PATIENTS AND METHODS

The Human Research and Ethics Committee of the Soroka Medical Center in Beer Sheva, Israel approved this study.

*The first two authors contributed equally to the study

Table 1. Demographic data (see text explanation)

Variable	HFNC (Group 1, N=34)	NRB (Group 2, N=33)	*P*
Age (yr) (mean ± SD)	51.93 ± 23.1	60.12 ± 16.41	NS
Gender (M:F) (n)	21:13	21:12	NS
APACHE II score (mean ± SD)	23.9±6.1	24.1±6.0	NS
Sepsis/SIRS* (n)	12	16	NS
Abdominal	8	16	
Pulmonary	4	–	
Trauma** (n)	15	10	NS
Head trauma	6	2	
Chest trauma	2	2	
Abdominal	5	2	
Extremities	2	2	
Pelvis and spine	1	2	
Pancreatitis (n)	1	1	NS
Other (n)	6	6	NS
ICU days on mechanical ventilation before extubation (mean ± SD)	6.76 ± 4.6	6.3 ± 4.87	NS

* The diagnostic criteria for Sepsis/SIRS were based on the international consensus of the Survival Sepsis Campaign [6]

** Most of the trauma patients had multiple body system involvement on admission, with variable prevalence and clinical significance

PATIENTS

The study population consisted of mechanically ventilated patients hospitalized in a 12-bed medical/surgical ICU between June 2009 and December 2010 [Table 1].

All adult (age > 18 years) patients hospitalized during 2009–2010, without tracheostomy or chronic pulmonary disease, who were mechanically ventilated and underwent the weaning process and subsequent extubation were included in the study. Excluded were all patients with known chronic obstructive lung disease (COPD), obstructive sleep apnea, and asthma, who died prior to extubation or who underwent tracheostomy before extubation. COPD was defined as chronic lung disease in patients with a history of COPD exacerbations or documented confirmation of chronic airway obstruction via prior pulmonary function tests.

PROCEDURES

Every patient in the study was ventilated on assist-control mechanical ventilation mode (AC mode) prior to the weaning process. Ventilator parameters were set according to a tidal volume of 6 ml/kg, respiratory rate of 12 breaths/min and positive end-expiratory pressure (PEEP) of 5 cm H_2O. The inspired oxygen fraction (FiO_2) was dependent on arterial blood oxygen saturation parameters (goal saturation > 90%). The weaning process was initiated on pressure support ventilation whenever the patient reached the appropriate clinical conditions, such as full consciousness, cardiovascular stability, normothermia and FiO_2 of 0.5 or less (with arterial blood saturation > 90%). The patient was extubated after full consciousness was restored; the patient demonstrated a good cough reflex, cardiovascular stability, and adequate respiratory parameters with spontaneous breathing. Adequate respiratory parameters were defined as $FiO_2 \leq 0.5$, respiratory rate < 30/min, negative inspiratory pressure ≥ -25 cm H_2O, and a tidal volume of at least 3 ml/kg on pressure support of 5 cm H_2O for at least 30 min. Re-intubation was defined as intubation performed after extubation in patients with imminent muscular fatigue (defined as rapid shallow breathing, respiratory rate > 30/minute, and use of accessory muscles of respiration in the neck and upper body with associated tachycardia and elevated systemic arterial blood pressure), psychological discomfort, or inability to protect the airway and/or clear secretions in the 24 hour period after extubation.

The patients were allocated to two study groups according to the oxygenation device used after extubation. Group 1 comprised 34 patients treated with HFNC and Group 2, 33 patients treated with non-rebreathing (NRB) oxygen face mask (non-Venturi). The method of treatment was based on the availability of HFNC since there were insufficient HFNC devices for delivery to all patients in the ICU.

The control of FiO_2 was achieved by using an oxygen-air mixed device (BIRD® air-oxygen blender, Thermo Respiratory Group, USA). The HFNCs delivered 30 L/min flow rate of humidified warmed oxygen to the patients. The oxygen-air mixer was set to 100% O_2 immediately post-extubation and was later adjusted to maintain a goal arterial blood O_2 saturation > 90%. The NRB delivered 15 L/min of oxygen. As with the HFNC group, the oxygen-air mixer was set to 100% O_2 immediately post-extubation and was later adjusted to maintain a goal arterial blood O_2 saturation > 90%.

VARIABLES AND MEASURES

The MetaVision® Clinical Information System for ICUs (iMDsoft®, Israel) was used for retrospective analysis of all available clinical data. Vital parameters including heart rate, blood pressure, respiratory rate, PaO_2/FiO_2 ratio, FiO_2 ratio and PEEP just prior to extubation were obtained from the patients' electronic charts (MetaVision® Clinical Information System) for the period extending from 6 hours before extubation to 6 hours after extubation. Arterial blood gases were drawn and analyzed 1 hour prior to extubation and 1 hour after extubation.

The outcome variables included improvement in oxygenation (PaO_2/FiO_2), ventilation-free days, percentage of patients requiring re-intubation, length of ICU stay, and death in the ICU.

DATA ANALYSIS

Statistical evaluation of the results was done with the SPSS 18 package (SPSS Inc., Chicago, IL, USA). Normally distributed

data and continuous variable are presented as mean ± standard deviation (SD). Statistical comparisons between the two study groups for parametric data were conducted using the Kruskal-Wallis, Mann-Whitney and Student's *t*-test. Parametric variables are presented as mean and SD.

The outcome variables of ventilation-free days, percentage of patients requiring re-intubation, length of ICU stay, and death in the ICU were non-parametric. These data were analyzed with a 2 x 2 contingency table and a Fisher's exact test. Statistical significance was defined as $P < 0.05$.

RESULTS

Two hundred patients were mechanically ventilated during the study period. Of these, 133 were excluded from the study according to the exclusion criteria. The final study population comprised 67 critically ill patients who underwent gradual pressure support weaning and were extubated when clinically appropriate. There were no statistically significant differences in demographic data between group 1 and group 2 in age (51.9 ± 23.1 vs. 60.1 ± 16.4 years, respectively, $P > 0.1$) or male/female ratio (21:13 vs. 21:12, $P > 0.1$) [Table 1].

There was a higher rate of trauma in group 1 and higher rate of sepsis in group 2 [Table 1], but these differences were not statistically significant. There were no difficulties in the weaning process prior to extubation in either study group. The number of days on mechanical ventilation prior to extubation was not statistically significant between the study groups (6.8 ± 4.6 vs. 6.3 ± 4.9, $P = 0.69$).

There were no significant changes in $PaCO_2$ levels and PaO_2/FiO_2 before or after extubation between the groups ($P > 0.1$ respectively) [Table 2]. There were no significant differences between the groups in heart rate or mean arterial blood pressure after extubation [Table 2].

Table 2. Comparison of blood gas and hemodynamic parameters between the study groups

Variable	HFNCs (n=34)	NRB (n=33)	*P* value
PO_2/FiO_2 ratio Before extubation After extubation	 224.4 ± 73.2 270.5 ± 97.9	 256.8 ± 73.7 183.9 ± 61.8	 NS ‹ 0.0001
$PaCO_2$ levels (mmHg) Before extubation After extubation	 42.7 ± 6.2 39.7 ± 6.1	 38.3 ± 7.3 40.4 ± 6.1	 NS NS
Respiratory rate/min Before extubation After extubation	 14.3 ± 2.2 20.7 ± 5.3	 16.7 ± 3.9 20.4 ± 5.4	 NS NS
Mean arterial pressure (mmHg) Before extubation After extubation	 81.2 ± 11.5 91.1 ± 11.5	 90.8 ± 13.5 94.8 ± 16.9	 NS NS
Heart rate (beats/min) Before extubation After extubation	 94.4 ± 19.2 98.6 ± 16.5	 89.5 ± 16.1 94.9 ± 14.1	 NS NS

Values are presented as mean ± SD

The PaO_2/FIO_2 ratio values were similar in the two groups prior to extubation ($P < 0.1$) [Table 2]. However, after extubation the mean PaO_2/FiO_2 ratio increased significantly after extubation in the HFNC group (224 vs. 270, $P < 0.05$). In contrast, in the NRB masks group the mean PaO_2/FiO_2 ratio significantly decreased after extubation (256 vs. 183, $P < 0.05$) [Table 2]. Finally, there was an immediate significant improvement in oxygenation using HFNC compared to NRB masks (270 vs. 183 mmHg, $P < 0.0001$) after extubation [Table 2].

There was a significantly higher number of ventilator-free days in the HFNC group ($P < 0.03$) [Table 3] and a significantly lower rate of re-intubation in the HFNC group (1 vs. 6, $P = 0.04$). There were no significant differences between the groups in ICU length of stay or survival. Non-invasive ventilation was not used in either study group prior to re-intubation.

DISCUSSION

Extubation failure continues to be a major issue for ventilated critically ill patients [13]. Choosing the appropriate device for respiratory support after extubation may improve the chances of weaning and ultimately the overall clinical outcome. This study compared two devices that can be utilized after extubation: HFNC and NRB. We demonstrated significant clinical advantages for HFNC including better oxygenation, reduced need for re-intubation, and increased ventilation-free days. Achieving better oxygenation with HFNC is well described in previously published clinical trials in pediatrics [9-12] and adult populations [8,14-17].

Our data also showed a significantly lower requirement for re-intubation (1 of 34 patients, 3%) in the HFNC group compared to the NRB group (6 of 33 patients, 18%). The re-intubation rate in the NRB group (6 of 33 patients, 18%) correlated well with previously published data (10–19%) [18]. The re-intubation requirement in ICU after extubation failure correlated with a high rate of ICU mortality (up to 50%), new-onset nosocomial pneumonia (up to 30%), longer ICU stay

Table 3. Comparison of clinical outcomes between the study groups

Variable	HFNCs (n=34)	NRB (n=33)	*P* value
Ventilator-free days* (mean ± SD)	4.14 ± 2.2	3.0 ± 2.0	0.03**
Re-intubation (n)	1/34	6/33	0.04**
Days in ICU (mean ± SD)	10.7 ± 6.2	10.5 ± 7.3	NS
Mortality (n)***	1/34	0/33	NS

* Ventilator-free days were defined as days alive and free from mechanical ventilation during the ICU stay

** More ventilator-free days were demonstrated in the HFNC group compared to the NRB group ($P < 0.05$). Significantly fewer re-intubations were required in the HFNC group ($P < 0.05$)

*** In-ICU mortality rate

HFNC = high flow nasal cannula, NRB = non-breathing face mask, ICU = intensive care unit

and mechanical ventilation [19], and need for long-term care and rehabilitation [20]. In our study no significant change in mortality was found between the groups during the ICU stay, but we had no available data regarding in-hospital and long-term mortality.

Interestingly, the vast majority of re-intubated patients in the NRB group had a diagnosis of sepsis on admission, whereas most of the patients in the HFNC group were trauma patients. These findings may suggest a higher efficacy of HFNC in trauma-related respiratory failure and might be explained by differences in primary pathophysiological mechanisms of acute lung injury in trauma and non-trauma patients. Thus, Ware et al. [21] found a significantly low rate of endothelial injury in ARDS/ALI (acute respiratory distress syndrome/acute lung injury) trauma patients compared to other ICU populations. However, the difference in prevalence of sepsis or trauma in either group was not statistically significant.

HFNC appears to be an effective new therapeutic option compared with other oxygen delivery devices (non-rebreathing oxygen masks, high humidity face masks, high humidity tracheostomy collars, Venturi mask, etc.). The major benefits of HFNC include continuous alveolar recruitment and reduction of airway collapse (effect of continuous positive airway pressure, CPAP). Achieving both of these physiological effects are key factors in achieving adequate minute ventilation and sufficient oxygenation [13]. Interestingly, several randomized clinical trials [22-24] using different non-invasive ventilation (NIV) respiratory devices demonstrated a reduced incidence of post-extubation pneumonia and re-intubation, improved weaning, and reduced length of hospital stay. Such benefits of NIV are likely related to the similar physiological effects observed when applying CPAP during the early post-extubation period. However, the efficacy of HFNC devices to prevent re-intubation in extubated patients has not been previously well studied.

Other benefits of HFNC include the preservation of mucosal function and reducing tracheal secretions by using heated and humidified oxygen [14]. Furthermore, the use of HFNC allows for the patient's uninterrupted ability to eat or talk as compared with other more restrictive oxygen delivery devices.

Among the reported disadvantages related to HFNC is cost of the device [14,15]. There is also a potential risk of microbial colonization in the humidified delivery system. However, there have been no clinical reports to significantly associate the use of humidified HFNC and increased pulmonary infections.

The primary limitations of this study were the small population size (n=67) and its observational and retrospective study design. In view of the retrospective design there are no consistent clinical data regarding the long-term outcomes of patients during the hospital stay and after discharge. Another potential limitation may be related to differences in the groups since more septic patients were in the NRB group (although this difference was not statistically significant).

The clinical implications of our results are quite promising. Choosing the most appropriate respiratory support device in the immediate post-extubation period may ultimately improve the immediate oxygenation, and may impact the later need for re-intubation and ultimately the patient's outcome.

The results of this small observational study should be interpreted with caution and should inspire future prospective studies with a larger patient population. Hopefully, ensuring a more homogeneous population in the study groups will diminish the "selection bias" of the present study. Such studies might include patients with chronic lung disease (COPD, asthma, obstructive sleep apnea, etc.) to clarify the potential usefulness of HFNC for such patients.

CONCLUSIONS

High flow nasal cannula is an effective and beneficial method of oxygen delivery in extubated patients compared with the non-rebreathing oxygen mask. It may reduce the need for re-intubation, increase ventilation-free time, and significantly improve oxygenation in the post-extubation period in critically ill patients in the ICU. We strongly recommend the routine use of HFNC as a means of preventing re-intubation and mechanical ventilation in the general critically ill population.

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