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Comparison of high flow oxygen therapy versus noninvasive mechanical ventilation for successful weaning from invasive ventilation in children

An observational study

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Abstract

Post-extubation respiratory failure is associated with a poor prognosis due to increased ventilator-associated pneumonia, and longer length of stay in the ICU and hospital. In this study, we aimed to evaluate the efficacy of high-flow nasal cannula (HFNC) and noninvasive mechanical ventilation (NIMV) on extubation success in children. A total of 48 patients, aged between 1 month and 18 years, who were weaned to either NIMV or HFNC were included. Patients who had tracheostomy or were not weaned and underwent unplanned extubation were excluded. Age, gender, anthropometric parameters, Pediatric Risk of Mortality and Pediatric Logistic Organ Dysfunction scores, oxygenation index, mechanical ventilation length of stay (LOS), HFNC/NIMV LOS, Modified Downes-Silverman score (MDS), and venous blood gas parameters, pediatric intensive care unit (PICU) LOS were recorded. 24 patients were extubated to NIMV, and 24 patients to HFNC. HFNC LOS and NIMV LOS were similar ($P = .621$). The failure rates at the 48th hour of HFNC and NIMV were 33% (n = 8), and 33% respectively (n = 8) ($P = 1.0$). PICU LOS and mortality rate was also similar ($P = .06$, $P = .312$ respectively). MDS decreased significantly in both groups ($P < .001$, $P = .02$ respectively). Changes in blood gas parameters and MDS within the first 48-hour of device application were similar between the 2 groups. HFNC is not inferior to NIMV in patients with extubation difficulty or those expected to have such difficulty in terms of treatment success, PICU LOS, and mortality. Therefore, HFNC appears to be a weaning technique alternative to NIMV after extubation.

Abbreviations: CPAP = continuous positive airway pressure, HFNC = high-flow nasal cannula, IMV = invasive mechanical ventilation, LOS = length of stay, MDS = Modified Downes-Silverman score, NIMV = noninvasive mechanical ventilation, PERF = post-extubation respiratory failure, PICU = pediatric intensive care unit.

Keywords: critical care, high-flow nasal cannula, non-invasive ventilation, pediatric, weaning

1. Introduction

Post-extubation respiratory failure (PERF) develops after 10% to 20% of planned extubations and is associated with a poor prognosis due to increased ventilator-associated pneumonia, and longer length of stay in the ICU and hospital.[1] The reintubation rate can be as high as 20% to 35% in high-risk adult patients,[2,3] and it is also an independent risk factor for poor prognosis in adults.[4]

Non-invasive mechanical ventilation (NIMV) has been used in acute respiratory failure and in PERF. Post-extubation use of NIMV is known to reduce reintubation rates in both adults and children.[5–8] Although providing improvement in extubation success, it has several complications such as nasal trauma, mask-related pressure ulcers, use of sedatives to improve patient tolerance, and a need for more nursing staff to assist in the delivery of the device.[8,9]

High-flow nasal cannula (HFNC) emerged as an alternative that has been used in PERF through a reduction in respiratory workload and enhancement of oxygenation. HFNC reduces inspiratory resistance associated with the nasopharynx by providing a nasopharyngeal flow rate greater than the inspiratory flow rate of the patient; increasing alveolar ventilation by washing out nasopharyngeal dead space; improving pulmonary compliance and conductance by providing an adequate quantity of humidified and heated air, and provides a positive expansion pressure for the lungs.[10,11] Extubation to HFNC has been reported to be as effective as NIMV, mostly in adults and

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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neonates.[12–14] In the current study, we aimed to compare the efficacy of HFNC and NIMV on extubation success in pediatric patients.

2. Methods

2.1. Patients

The study was conducted in the Pediatric Intensive Care Unit (PICU) of a tertiary referral center with a 16-bed capacity for both medical and surgical patients. The study protocol was approved by the Hacettepe University Ethics Committee (GO15/661 2015/09). Informed consent was waived due to the retrospective nature of the study.

Patients, aged between 1 month and 18 years, who were weaned to either NIMV or HFNC between 2009 and 2018 years were reviewed retrospectively. Patients who had a tracheostomy, were not weaned and underwent unplanned extubation, or, had a history of prematurity and associated bronchopulmonary dysplasia, and those in need of oxygen therapy due to chronic pulmonary diseases were excluded from the study.

In order to evaluate the effect of primary disease on extubation success, patients were classified into 5 sub-groups: postoperative congenital heart diseases, neuromuscular diseases, parenchymal lung diseases, airway pathologies and thorax deformities/abnormalities, and others.

2.2. NIMV protocol

NIMV was performed with the ICU ventilation device (Engström Carestation, GE Healthcare) in NIMV mode using a facemask. Continuous positive airway pressure (CPAP) or bilevel positive airway pressure modes were used during NIMV. For the NIMV-treated patients under bilevel positive airway pressure mode, inspiratory positive airway pressure was initially set as 7 cm H_2O and the expiratory positive airway pressure as 3 to 4 cm H_2O in order to improve patient compliance, and later increased incrementally by 1 to 2 cm H_2O to the target 6 to 8 mL/kg of tidal volume. Under the CPAP mode, the initial pressure was set as 7 cm H_2O. Pressure and FiO_2 changes were based on the blood gas, saturation, and respiratory distress symptoms of the patients.

2.3. HFNC protocol

The HFNC device (AIRVO2, Optiflow, Fisher & Paykel Healthcare, New Zealand) comprised a system that delivers flows of air/oxygen mixtures from 0.21 to 1.00 of FiO_2 and 2 to 60 L/min of air with a heater and a humidifier. A gas mixture at 34°C was delivered to the patient over the inspiratory circuit through a nasal cannula. For patients under HFNC, the initial flow rate was set as 2 L/kg/min in infants and 1 L/kg/min in children. The flow rate was changed based on the respiratory distress of the patient (retraction, nasal flaring, thoracoabdominal asynchrony, tachypnea). FiO_2 was initially set as 0.4 and then adjusted so as to achieve a minimum of 92% saturation in the patient.

2.4. Data collection

Age, gender, the reason for intubation, Pediatric Risk of Mortality[15] and Pediatric Logistic Organ Dysfunction scores,[16] inotrope score (Dopamine dose [μg/kg/min] + Dobutamine dose [μg/kg/min] + 100 × Epinephrine [μg/kg/min]), oxygenation index, invasive mechanical ventilation (IMV) modes, IMV length of stay (LOS) before HFNC/NIMV, NIMV modes, HFNC or NIMV LOS, PICU LOS, and complications during NIMV or HFNC (atelectasis, pneumothorax, pneumomediastinum) detected through anterior-posterior lung X-ray images taken within 24 hours following HFNC or NIMV were recorded. Height, weight, and malnutrition z-scores at admission to PICU were recorded. For the malnutrition z score, the weight-for-height z-score was used for children aged under 2 years, and the body mass index z-score was used for patients aged over 2 years of age.[17]

The purpose-built "Modified Downes-Silverman score (MDS)," assessing the changes in respiratory distress symptoms of the patients, is composed of 6 sections with 3 Likert scale. Intercostal/sternal retraction, thoracoabdominal asynchrony, peak heart rate, cyanosis (saturation), respiratory rate, and state of consciousness parameters were scored between 0 and 2 and summed for each patient. Increasing scores indicated worsening of respiratory symptoms.

Venous blood gas parameters (PO_2, and PCO_2) and FiO_2 immediately before HFNC/NIMV and at 1, 6, 12, 24, and 48 hours after initiation of HFNC/NIMV, and MDS scores at 1, 6, 12, 24, and 48 hours after initiation of HFNC/NIMV were recorded.

2.5. HFNC/NIMV outcome

HFNC-treated patients were switched to NIMV or reintubation and NIMV-treated patients were reintubated based on any impairment in blood gas parameters (a gradual increase of PCO_2, inadequate arterial oxygenation, that is, $FiO_2 > 0.6$ with $PO_2 < 70$, or $FiO_2 > 0.6$ with cyanosis), signs of respiratory distress (subcostal/supraclavicular retraction, thoracoabdominal asynchrony, nasal flaring). Switching to NIMV or reintubation within 48 hours after extubation was considered a failure for HFNC-treated patients. Reintubation within 48 hours after extubation was considered a failure for NIMV-treated patients.

2.6. Statistical analysis

Data were analyzed with the package program SPSS for Windows 11.5. Descriptive statistics for normally distributed variables are shown as mean ± standard deviation, and for non-normally distributed variables as median (min-max); nominal variables are shown as number of cases and percentage (%). Mean values of continuous variables are compared using t tests; medians are compared using the Mann–Whitney U test or the Wilcoxon test, as appropriate. For more than 2 groups, mean values of continuous variables are compared using ANOVA variance analysis; medians are compared using the Kruskal-Wallis test. Nominal variables were assessed using Pearson Chi-square or Fisher exact test. The change in blood gas parameters and MDS score within 48-hour of HFNC/NIMV was investigated using repeated measures analysis. A P value <.05 is considered to be statistically significant.

3. Results

3.1. The main characteristics of the patients

Forty-eight patients were included in the study; 24 patients were extubated to NIMV and 24 to HFNC. The main characteristics of the patients are presented in Table 1. There were no differences between the 2 groups in terms of gender, age, and malnutrition z-score (P = .771, P = .252, and P = .614, respectively) (Table 1). The most common reason for intubation was respiratory infections. Mechanical ventilation mode before HFNC/NIMV, IMV LOS, oxygenation index, inotrope score, Pediatric Risk of Mortality, and Pediatric Logistic Organ Dysfunction score were similar between the groups (Table 1). Median MDS 1-hour score was similar between the HFNC and NIMV groups (P = .07) (Table 1).

3.2. The outcome of the HFNC and NIMV groups

The median HFNC LOS was 4 days (1-20), and the NIMV LOS was 3 days (1-18) (P = .621). The median HFNC or NIMV LOS were also similar between patients with treatment success (P = .470) (Table 2).

The failure rates at the 48th hour of HFNC and NIMV were 33% (n = 8), and 33% (n = 8) (P = 1.0), and at the 28th day 37% (n = 9) and 54.1% (n = 13) respectively (P = .246). Twenty percent (n = 5) of the HFNC-treated patients were switched to NIMV, and 16% (n = 4) of the HFNC-treated patients were reintubated at the 28th day (Table 2).

The MDS scores of the HFNC and NIMV groups decreased significantly in the first 48th hour of HFNC/NIMV (P < .001, P = .02, respectively). The magnitude of improvement in the MDS score was similar between the HFNC and NIMV groups (F = 3.095, P = .091). There was also no difference in the change of PCO2 (F = .035, P = .853), PO2 (F = .417, P = .529), and PO2/FiO2 (F = .171, P = .686) within the first 48 hours of device application between the 2 groups.

3.3. Complications

None of the patients developed pneumothorax and pneumomediastinum during HFNC and NIMV. Atelectasis was detected in 29% (n = 7) of the HFNC group and 4.5% (n = 1) of the NIMV group (P = .132).

3.4. Mortality

ICU mortality was 4.2% (n = 1) in the HFNC group and 4.2% (n = 1) in the NIMV group (P = .999). One patient in the HFNC group died of cardiogenic shock and 1 patient in the NIMV group died of acute respiratory distress syndrome (ARDS).

3.5. Sub-group analysis

There was no difference between the diagnostic subgroups in terms of HFNC and NIMV success (Table 3). HFNC/NIMV LOS, PICU LOS, and PICU LOS after the initiation of HFNC/NIMV were similar between the groups (Table 3).

4. Discussion

In this study, which evaluated the successful weaning from invasive ventilation in children, no difference was found in HFNC and NIMV success rates in terms of PICU LOS, PICU LOS after initiation of the device, and mortality. The MDS scores decreased significantly in both groups, and there was no difference in the change in blood gas parameters and MDS between the 2 groups.

Easy application and patient tolerance of HFNC have led to its use for various respiratory conditions. Although indications have included mostly acute bronchiolitis, asthma, sleep apnea, pneumonia, and transport of a critical patient in order to avoid invasive mechanical ventilation, it has increasingly been used

Table 1

The main characteristics of the patients in the HFNC and NIMV groups.

Variables	HFNC group (n = 24)	NIMV group (n = 24)	*P*
Age, mo, median (range)	16 (3-168)	23 (4-165)	.252
Male sex, number, (%)	14 (58%)	13 (54.2%)	.771
Malnutrition, z score, median (range)	-0.5 (-3.9-3.2)	-1.9 (-3.9-3.2)	.614
Reason for intubation	17 (71)	15 (63)	.565
Respiratory infection, n (%)	3 (12)	7 (29)	
Respiratory depression, n (%)	4 (17)	2 (8)	
Postoperative, n (%)			
Mechanical ventilation mode	22 (92%)	18 (75%)	.282
SIMV-P, n, (%)	1 (4%)	2 (8.3%)	
SIMV-V, n, (%)	1 (4%)	4 (16.7%)	
SIMV-P/HFO, n, (%)			
IMV LOS, day, median (range)	9 (3-39)	16 (4-41)	.071
Inotrope score, median (range)	0 (0-9)	2.5 (0-10)	.147
PRISM score, median (range)	11.5 (2-29)	14.5 (2-29)	.111
PELOD score, median (range)	12 (1-30)	12 (1-31)	.625
OI, median (range)	8.87 (5.5-20)	9.9 (6-36)	.166
MDS 1-h, median (range)	6.0 (5-9)	7.0 (4-9)	.178

HFNC = high flow nasal cannula, HFO = High Frequency Oscillation, IMV = invasive mechanic ventilation, LOS = length of stay, MDS = Modified Downes-Silverman score, NIMV = noninvasive mechanic ventilation, OI = Oxygenation index, PELOD = Pediatric Logistic Organ Dysfunction, PRISM = Pediatric Risk of Mortality, SIMV-P and -V = Synchronized intermittent mandatory ventilation -Pressure and–Volume.

Table 2

Outcome of the HFNC and NIMV groups.

Outcome	HFNC group	NIMV group	*P*
Device LOS, d, median (range)	4.0 (1-20)	3.0 (1-18)	.621
Device LOS with successful application, d, median (range)	5 (2-20)	5 (2-18)	.449
PICU LOS, d, median (range)	21 (11-68)	28.5 (5-54)	.060
PICU LOS after initiation of device, d, median (range)	11.5 (3-49)	17 (1-39)	.212
Failure rate, 48thh, n (%)	8 (33%)	8 (33%)	1.0
Failure rate, 28th d, n (%)	9 (37.5%)	13 (54.2%)	.191
PICU mortality, n (%)	1 (4.2%)	1 (4.2%)	.312
Atelectasis, n (%)	6 (25%)	1 (4.5%)	.132

HFNC = high flow nasal cannula, IMV = invasive mechanic ventilation, LOS = length of stay, NIMV = noninvasive mechanic ventilation, PICU = pediatric intensive care unit.

Table 3

Outcome of patients in the HFNC and NIMV groups according to the diagnostic sub-groups.

	HFNC/NIMV LOS, d, median (range)		PICU LOS, days, median (range)		PICU LOS after initiation of device, d, median (range)		Failure Rate, 48th h, n, (%)	
Diagnostic groups	**HFNC**	**NIMV**	**HFNC**	**NIMV**	**HFNC**	**NIMV**	**HFNC**	**NIMV**
Congenital heart disease, postop. (n = 10)	9.0 (1-20)	2 (1-6)	27.0 (15-53)	29 (16-47)	20 (13-25)	20 (5-37)	1 (33%)	3 (43%)
Neuromuscular disease (n = 7)	3 (1-4)	2 (1-3)	16.0 (13-30)	23.5 (13-54)	7 (4-23)	16 (6-32)	1 (33%)	2 (50%)
Parenchymal lung diseases (n = 11)	5 (1-7)	4.5 (2-15)	21 (13-42)	39.5 (5-49)	11 (6-20)	13 (1-25)	1 (20%)	0 (0%)
Airway pathologies and thorax deformities/ abnormalities (n = 11)	4 (2-12)	4.5 (2-7)	27 (11-68)	37 (28-46)	10 (3-49)	24.5 (10-39)	3 (33%)	1 (50%)
Others (n = 9)	3.5 (1-7)	7.5 (1-18)	16 (15-17)	29 (28-30)	10 (7-13)	19 (18-20)	2 (50%)	1 (25%)
P	.699	.331	.739	.885	.577	.858	.925	.238

HFNC = high flow nasal cannula, LOS = length of stay, NIMV = noninvasive mechanic ventilation, PICU = pediatric intensive care unit.

for post-extubation respiratory support. A higher flow rate than the inspiratory flow rate of the patient provides less dilution with room air, creating an airway pressure with an effect similar to CPAP, and increasing oxygen reserve by washing out the nasopharyngeal dead space.[18] HFNC reduces the respiratory workload and prevents the collapse of small airways, and thus contributes to oxygenation by reducing pulmonary shunts.[19,20]

Several studies showed a reduction in peak heart rate, and respiratory rate with the HFNC when compared to the conventional oxygen therapy.[14,21,22] Also, improvement was observed in markers that quantified hypoxia.[23] We detected an improvement in clinical symptoms of respiratory failure that was indicated by the MDS score in both groups, and the change in clinical symptoms and blood gas parameters was similar between the 2 groups. Although HFNC has been shown to be effective in the improvement of oxygenation,[19,21] its effect on patients with hypercapnia is controversial.[24,25] HFNC increases tidal volume by increasing lung impedance,[26] respiration turns into a slower and deeper pattern,[27] and thus the respiratory rate is reduced without any change to $PaCO_2$. Noninvasive ventilation is well established ventilatory modality to treat hypercapnic respiratory failure. Despite this well-known effect, pCO_2 change was similar between the 2 groups. Recent studies revealed improvement of ventilatory efficiency and reduction in the work of breathing in patients with hypercapnic respiratory failure who were put on HFNC.[28] However, further studies are needed to recommend HFNC for hypercapnic respiratory failure.

HFNC has been established as a useful tool for in infants with bronchiolitis and children with respiratory distress regarding decreased intubation rates.[29,30] Also, post-extubation use of HFNC has been exhibited effective in improvement of extubation success, however, studies mainly include neonates and adult patients.[1,13,31,32] Extubation to HFNC is better compared to conventional oxygen therapy in terms of restoration of respiratory parameters and reintubation rates.[23] Richter et al reported pediatric patients after cardiac surgery that were extubated to either positive airway pressure or HFNC, and extubation failure was similar between the 2 modalities.[33] In our study, the failure rate was similar between the HFNC (33%) and the NIMV (33%) groups and also compatible with the literature.[1,5,13,32,34–38] There was no difference in the HFNC and NIMV LOS between the 2 groups in our study similar to other studies in the literature.[38] The PICU LOS and mortality rates were reported mostly similar between extubation to HFNC and NIMV, some reports stated shorter PICU LOS with HFNC compared to CPAP.[39] We found similar PICU LOS and mortality rates between the 2 groups. All these data suggest that HFNC and NIMV may provide comparable support for PERF in pediatric patients.

Post-extubation atelectasis is typically observed in 10-30% of patients within the first 24 hours following extubation. HFNC increases end-expiratory lung volume by delivering flow rate-dependent PEEP.[40] Akyıldız et al reported a decrease in atelectasis during a 48-hour period in patients who were extubated to HFNC.[23] Corley et al reported no difference between patients who were extubated to HFNC after cardiac surgery and standard oxygen therapy on days 1 and 5.[40] We found a slightly higher frequency of atelectasis in the HFNC group.

Patients in the NIMV and HFNC groups were heterogeneous in terms of hypercapnic and hypoxic respiratory failure. Although we did not aim to evaluate the efficacy of HFNC and NIMV on hypercapnic and hypoxic respiratory failure, changes in PO2, PCO2, and PO2/FiO2 values were similar between the 2 groups. However, in the diagnostic subgroups that were more homogenous in terms of hypoxia and hypercapnia, the efficacy of HFNC and NIMV was similar. This situation is more important for the congenital heart disease group which had more probability of extubation failure due to the risk of pulmonary complications such as pulmonary edema, pulmonary infection, anatomic compression of the airway secondary to cardiac or vascular conditions, atelectasis, and pulmonary hypertension.

Our study had several limitations. First, a central venous catheter was used as a venous line for patients in our PICU. Blood gas of the patients was collected from this catheter and the PO_2, PCO_2, and PO_2/FiO_2 values were assessed accordingly. Though, these values were used for making comparisons between the groups and did not change the analysis results. Second, patients were heterogeneous in terms of hypercapnia and hypoxia, but sub-group analysis revealed the same efficacy. Third, our cohort consisted of a limited number of patients.

In conclusion, HFNC is not inferior to NIMV in patients with extubation difficulty or those expected to have such difficulty in terms of treatment success, IMV LOS, and mortality. Therefore, HFNC appears to be a weaning technique alternative to NIMV after extubation.

Authors' contributions

NBC contributed to the conception and design of the study. NBC, MT collected the samples. NBC, MT performed the statistical analysis. NBC, MT, FY, SK, BB wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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