Turkish Archives of Pediatrics

ORIGINAL ARTICLE
DOI: 10.5152/TurkArchPediatr.2024.23301

Comparison of the Efficacies of High-Flow Nasal Cannula Oxygen Therapy and Non-invasive Nasal Cannula Ventilation in Preventing Intubation

Ülkem Koçoğlu Barlas[1], Abdulrahman Özel[2], Volkan Tosun[3], Emine Ufuk Bozkurt[4], Hasan Serdar Kıhtır[5]

[1]Department of Pediatrics, Pediatric Intensive Care Unit, Göztepe Prof Dr Süleyman Yalçın City Hospital, İstanbul Medeniyet University Faculty of Medicine, İstanbul, Turkey
[2]Department of Pediatrics, Bağcılar Training and Research Hospital, University of Health Sciences, İstanbul, Turkey
[3]Mardin Research and Training Hospital, Mardin, Turkey
[4]Doğubeyazıt Dr Yaşar Eryılmaz State Hospital, Ağrı, Turkey
[5]Antalya Training and Research Hospital, University of Health Sciences, Antalya, Turkey

What is already known on this topic?

- *Non-invasive ventilation support is frequently used in pediatric intensive care units.*
- *There are few studies comparing the effectiveness of different interfaces in the pediatric age group.*

What this study adds on this topic?

- *In this study, a comparison was made between non-invasive respiratory support methods, and it was found that the intubation rate was higher in the group initially treated with nasal cannula non-invasive ventilation.*
- *High-flow nasal cannula oxygen therapy protects patients against intubation.*

ABSTRACT

Objective: This study aimed to compare high-flow nasal cannula oxygen therapy (nc-HFOT) and non-invasive nasal cannula ventilation (nc-NIV) in terms of intubation requirements.

Materials and Methods: The study was conducted retrospectively on cases followed up in the pediatric intensive care unit (PICU) between October 2019 and December 2021.

Results: Of all cases, 43 (55.8%) were male, and the median age was 16 months. The median PRISM-3 score for all cases was 2.5 (range: 0-3). Among the cases 45 cases (58.4%) received nc-HFOT treatment, and 32 cases (41.6%) received nc-NIV treatment. The median duration of respiratory support for all cases was 2 days, and 14 cases (18.2%) needed intubation. The median PICU stay day for all cases was 7 days, and the median hospital stay day was 11 days. The median age, PICU, and hospital stay days of the nc-NIV group were significantly higher ($P < .05$). In the logistic regression analysis, the probability of requiring intubation in cases initially nc-NIV was performed was found to be 4.95 times higher than those using nc-HFOT (OR: 4.95, 95% CI: 1.3-18.8, $P = 0.01$). Additionally, cases with underlying chronic diseases were found to have a 5.9 times increased likelihood of requiring intubation compared to those without (OR: 5.9, 95% CI: 1.41-24.5, $P = .01$). Five cases (6.5%) were lost during intensive care stay.

Conclusion: The application of nc-NIV increases intubation by 4.95 times compared to the application of nc-HFOT. The intubation rate in cases with underlying chronic diseases is also 5.9 times higher than those without.

Keywords: High-flow oxygen therapy, intensive care, intubation, nasal cannula, non-invasive ventilation, pediatric

INTRODUCTION

Respiratory system-related intensive care support treatments constitute a significant portion of those administered during childhood. The high risk of infection associated with invasive mechanical ventilation (IMV) support, the extension of intensive care stay, and side effects due to concurrently used sedatives have accelerated the shift toward non-invasive ventilation (NIV) support methods.[1] Therefore, high-flow nasal cannula oxygen therapy (nc-HFOT), continuous positive airway pressure (CPAP), and BiLevel positive airway pressure (BIPAP) have become alternative treatment methods that can replace IMV today.[2]

Corresponding author:
Ülkem Koçoğlu Barlas
✉ ulkemkocoglu@yahoo.com
Received: December 11, 2023
Revision Requested: January 12, 2024
Last Revision Received: January 18, 2024
Accepted: February 13, 2024
Publication Date: March 1, 2024

Cite this article as: Koçoğlu Barlas Ü, Özel A, Tosun V, Ufuk Bozkurt E, Serdar Kıhtır H. Comparison of the efficacies of high-flow nasal cannula oxygen therapy and non-invasive nasal cannula ventilation in preventing intubation. *Turk Arch Pediatr.* 2024;59(2):214-220.

High-flow nasal cannula oxygen therapy is a relatively safe and effective respiratory support method used in acute respiratory failure (ARF). It is known to increase lung compliance by eliminating dead space ventilation and enhancing mucociliary clearance, thereby reducing the patients' respiratory workload. Its efficacy as a rescue treatment, especially in moderate to severe bronchiolitis, has been confirmed.[3-5] In addition to bronchiolitis, it has been reported to be usable for pneumonia, asthma attacks, pre-intubation bridge therapy, and post-extubation support treatment.[6] Non-invasive ventilation uses positive pressure to improve oxygenation and ventilation, thereby reducing respiratory workload. While doing this, it uses various interfaces between the patient and the machine instead of an endotracheal tube. According to experience, 93% of children use nasal masks, 6% use oronasal or full-face masks, and 1% use other interfaces.[7,8] There is no data in the literature regarding the use of nasal cannula outside the neonatal period. It can be used in cases of both acute and chronic respiratory failure in all age groups. Non-invasive ventilation support used in ARF is known as a respiratory support method that prevents intubation with high success rates.[9,10]

The primary aim of this study is to compare cases that were treated with nc-HFOT and non-invasive nasal cannula ventilation (nc-NIV) due to ARF in terms of progression to intubation. In the study, the cases were assessed for the effectiveness and differences of the respiratory support methods applied in protecting the cases from intubation. The secondary aim of this study, on the other hand, was to identify other factors that lead to intubation.

MATERIALS AND METHODS

Study Design

The study included cases admitted to the 8-bed tertiary PICU between October 2019 and December 2021. In our PICU, only postoperative monitoring of cases undergoing cardiac surgery is not performed. Ethical approval was obtained from an external ethics committee of İstanbul Medeniyet University, Göztepe Training and Research Hospital Ethic Committee (approval number: 2022/0404, date: June 29, 2022) for the study, and was designed and conducted in accordance with the ethical principles set out in the Declaration of Helsinki. Inclusion criteria for the study were as follows: (i) being between 1 month to 18 years old, and (ii) receiving nc-HFOT or nc-NIV treatment due to ARF at any time during their PICU stay. Exclusions were nc-HFOT applied outside the PICU, cases younger than 1 month or older than 18 years, and cases whose data was missing. Acute respiratory failure was diagnosed using clinical and laboratory criteria: the presence of physical examination findings of respiratory failure for clinical criteria, such as tachypnea/bradypnea, wheezing, cyanosis, prominent retractions; and hypoxemia (partial arterial oxygen pressure [PaO_2] < 60 mm Hg with 60% Fraction of inspired oxygen [FiO_2], peripheral oxygen saturation [SpO_2] < 92%), and hypercapnia (partial carbon dioxide pressure [PCO_2] > 60 mm Hg) for laboratory criteria. Treatment success was defined as a decrease in respiratory rate, regression in retractions, decrease in FiO_2 needs, correction of hypoxemia and hypercapnia. Treatment failure was defined as intubation due to an increase in these parameters.

Respiratory Support Method Protocol

In our unit, nc-HFOT support is provided using the Airvo 2 (Fisher & Paykel Healthcare, Auckland, New Zealand) device. Although there is no written policy, the general practice is to start flow settings based on the patient's weight: 0-15 kg: 2 L/kg/min; 16-30 kg: 35 L/min; 31-50 kg: 40 L/min; >50 kg: 50 L/min. The starting FiO_2 value was determined based on the patient's SpO_2 value, and the minimum value that maintained SpO_2 between 92% and 97% was used. Nasal cannula selection was based on the patient's weight, initial flow rate, and size of the nasal aperture (Optiflow System®, OPT318, OPT842, OPT844, OPT846). The system temperature was monitored to be between 34°C and 37°C.

In our unit, nc-NIV support is applied using the Servo-I (Maquet Critical Care, Solna, Sweden) ventilation device. For the cases included in the study, the NIV pressure control (PC) mode of the device was used, and the positive end-expiratory pressure (PEEP), pressure above PEEP, respiratory rate (RR), FiO_2, and inspiration : expiration ratio (I:E) parameters were adjusted. Although there is no written policy, the general practice is to start with settings of 5-8 cmH_2O for PEEP, 10-12 cmH_2O for pressure above PEEP, and 1:2 for I:E. Decisions on the RR and FiO_2 were based on the patient's age, normal RR, PCO_2 value, and SpO_2 value. Nasal cannula selection was made based on the patient's weight and the size of the nasal aperture (Optiflow System®, OPT318, OPT842, OPT844, OPT846).

All cases were continuously monitored with electrocardiography, pulse oximetry, RR, and non-invasive arterial blood pressure. When necessary, sedation was achieved by intravenous ketamine infusion (1 mg/kg/h), intravenous midazolam infusion (0.1 mg/kg/h), and intravenous dexmedetomidine infusion (0.5 µg/kg/h). A nasogastric/orogastric tube was used in all patients both to prevent gastric distension and to provide feeding. If necessary, a urinary catheter was inserted to monitor urine output. Daily assessments were made, and in cases with a reduced respiratory workload, initially FiO_2, then the flow rate was reduced for nc-HFOT, and PEEP and pressure above PEEP were reduced for nc-NIV. When the support rates reached minimum values, the patient was separated from the device and placed on room air. Cases with an increased respiratory workload were intubated according to rapid sequential intubation rules.

Data Collection

Data for the cases was obtained retrospectively from hospital records. Data included demographic data (age, sex, ethnicity), acute illness diagnosis, presence of chronic illness, PICU and hospital stay, initial vital parameters (SpO_2, FiO_2, SpO_2/FiO_2 (S/F) ratio, PCO_2), applied respiratory support method, duration, and parameters (for nc-HFOT: peak flow/day, peak FiO_2/day, and RR; for nc-NIV: peak PEEP, average PEEP, peak FiO_2, and average RR), intubation status, if available, respiratory pathogen panel (RPP) result, applied treatments (inhaler treatment, systemic steroid, magnesium), Pediatric Risk of Mortality-3 (PRISM-3) score, and discharge-mortality status. Due to the retrospective nature of the study, no consent was obtained from patients or their guardians. Groups were defined as nc-HFOT and nc-NIV. Groups were equalized according to PRISM-3.

Statistical Analysis

Continuous variables were presented as median and interquartile range (25-75 percentiles). Categoric variables were presented as n (%). Kolmogorov–Smirnov test and Q–Q graph were used to examine the normality of the continuous variables. According to the normality analysis, Mann–Whitney *U*-test or *t*-test was used to compare continuous variables between 2 groups. Chi-square or Fisher's exact test was used for the comparison of categorical variables between 2 groups. Single and multivariable logistic regression analysis were used to identify factors associated with intubation requirement. Age (months), respiratory support time (days), peak flow (L/min), mean PEEP (cmH_2O), peak PEEP (cmH_2O), PRISM-3, chronic illness, and respiratory support type (HFOT/NIV) parameters were tested in single variable logistic regression, and variables found to be significant were then subjected to multivariable logistic regression analysis. Hosmer–Lemeshow test was used to assess the goodness of fit of the logistic regression model. A $P < 0.05$ was considered significant. The Statistical Package for the Social Sciences for Windows, Version 24.0 (IBM Corp., Armonk, NY) software was used for the statistical calculations.

RESULTS

Out of the 675 cases monitored in the PICU during the specified date range, 103 cases (15.2%) that met the inclusion criteria were included in the study. Of the cases, 26 cases were excluded from the study because more than one respiratory support method (both nc-HFOT and nc-NIV) were provided and/or had data limitations. The study continued with 77 cases (Figure 1). A total of 45 of the cases (58.4%) received nc-HFOT, and 32 (41.6%) received nc-NIV. Of all cases, 43 of them (55.8%) were male, and their median age was 16 months (range: 5-35 months). The median PRISM-3 score for all cases was 2.5 (range: 0-3), the initial SpO_2 value was 92% (range: 88%-95%), the initial PCO_2 value was 49 mmHg (range: 43-55), and the initial FiO_2 value was 50% (range: 45%-57.5%). The median duration of respiratory support for all cases was 2 days (range: 2-4 days), and 14 (18.2%) of them required IMV support. The median PICU stay for all cases was 7 days (range: 5-14 days), and the hospital stay was 11 days (range: 8-16 days). Table 1 represents the comparison of the general characteristics, vital parameters before treatment, and applied respiratory support methods for both groups. As shown, the median age value of the nc-NIV group was significantly higher ($P < .05$). Similarly, the PICU and hospital stay duration was longer in the nc-NIV group ($P < .05$). Acute respiratory failure was observed in 73 cases (94.8%) due to respiratory tract-related disorders, in 2 cases (2.59%) due to trauma and other surgical reasons, and in 2 cases (2.59%) due to sepsis. Thirty-six cases (46.8%) had at least 1 underlying chronic disease (Table 2). Five cases (6.5%) died during the intensive care stay.

i-square test results showed that the presence of chronic disease (n = 11, 78% vs. n = 25, 39.7%) and the use of nc-NIV (n = 10, 71.4% vs. n = 22, 34.9%) were higher in cases requiring intubation ($P = .08$ and $P = .01$, respectively). In the logistic regression analysis conducted, the application of nc-NIV and the presence

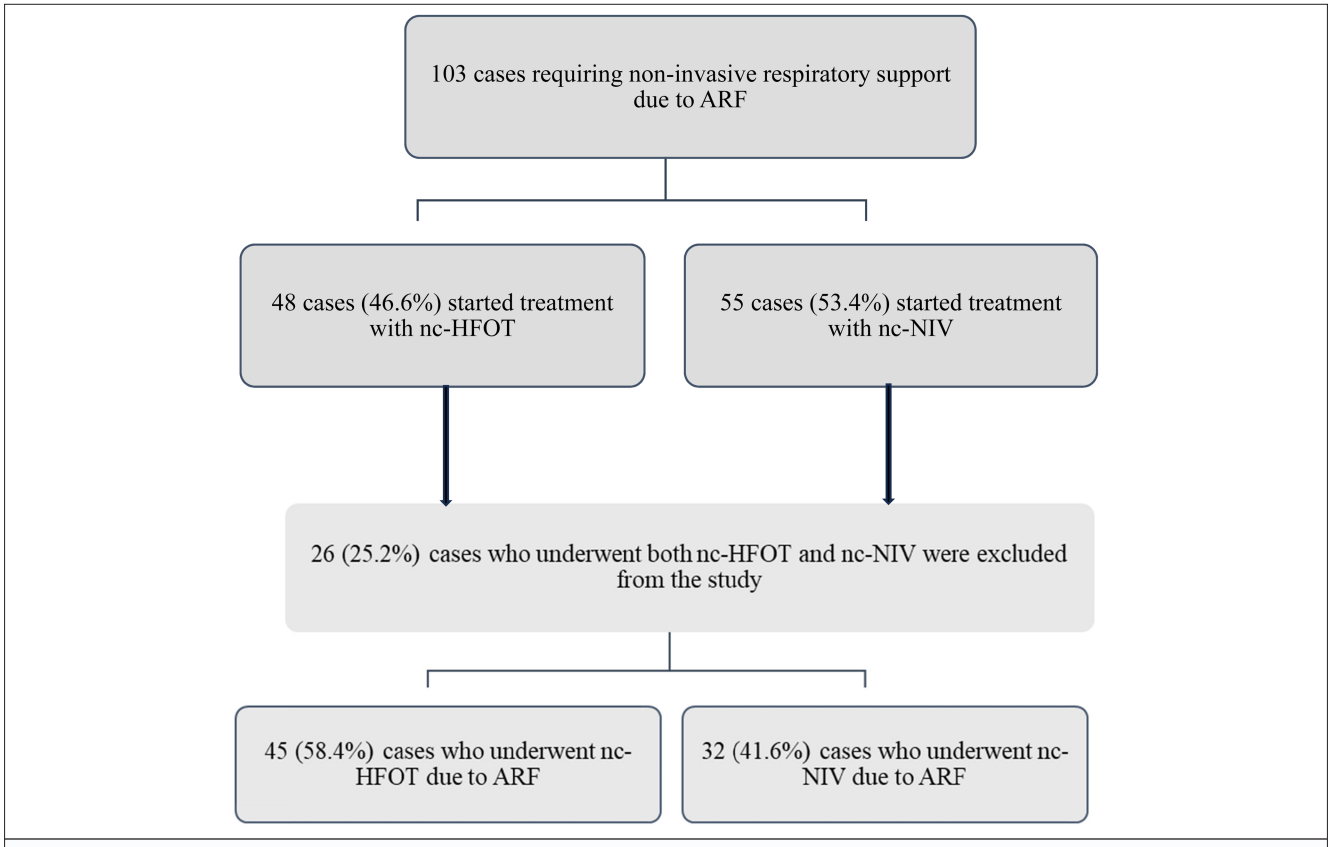

Figure 1. The diagram of the study .

Table 1. General Characteristics, Vital Parameters Before Respiratory Support and Respiratory Support Parameters of the Groups[#]

	nc-HFOT versus nc-NIV						
	nc-HFOT, (n = 45)			nc-NIV, (n = 32)			
	Median	25.p	75.p	Median	25.p	75.p	*P*
General characteristics							
Age (month)	11	3	21	23.5	9.5	60	**.008***
Prism-3	0	0	3	2.5	0	3	.07
PICU stay (day)	6	5	8	9.5	5.5	20	**.01***
Hospital stay (day)	10	7	13	15.5	10	22	**.001***
Vital parameters							
SpO2 (%)	92	88	94.5	93	90	95	.2
FiO2 (%)	50	45	65	50	45	55	.13
S/F (%)	174.45	128.13	208.89	192.00	165.45	213.33	.12[+]
Mean RR	23.5	22	25	20	20	23	.28
Respiratory support parameters							
Respiratory support time (day)	2	2	4	3	2	5	.37
Peak flow (L/min)	10	8	15				
Peak FiO2 (%)	50	45	55	45	45	52.5	.38
Peak PEEP (cmH_2O)				8	8	8	
Mean PEEP (cmH_2O)				8	7	8	

FiO2, fraction of inspired oxygen; nc-HFOT, nasal cannula-high flow oxygen therapy; nc-NIV, nasal cannula-noninvasive ventilation; PCO2, partial carbon dioxide pressure; PEEP, positive end-expiratory pressure PICU, pediatric intensive care unit; Prism-3, pediatric risk of mortality score-3; RR, respiratory rate; S/F, SpO2/FiO2; SpO2, peripheral oxygen saturation.
*$P < .05$.
[+]*t*-test.
[#]Kolmogorov–Smirnov test and Q–Q graph.

Table 2. Comparison of the Groups[#]

		nc-HFOT	nc-NIV	
		n (%)	n (%)	*P*
Sex	Male	23 (51.1)	20 (62.5)	.32
	Female	22 (48.9)	12 (37.5)	
Intubation	(-)	41 (91.1)	22 (68.8)	**.01***
	(+)	4 (8.9)	10 (31.3)	
Ethnicity	Migrant	21 (46.7)	13 (40.6)	.59
	Turkish	24 (53.3)	19 (59.4)	
Acute illness	Respiratory tract-related disorders	44 (97.8)	29 (90.6)	.319
	Trauma and other surgical cases	-	2 (6.3)	
	Sepsis	1 (2.2)	1 (3.1)	
Chronic illness	(-)	25 (55.6)	16 (50)	.63
	(+)	20 (44.4)	16 (50)	
Respiratory pathogen panel	(-)	31 (68.9)	21 (65.6)	.76
	(+)	14 (31.1)	11 (34.4)	
Inhaled beta2 agonist	(-)	8 (17.8)	8 (25)	.44
	(+)	37 (82.2)	24 (75)	
Iv Corticosteroid	(-)	13 (28.9)	13 (40.6)	.28
	(+)	32 (71.1)	19 (59.4)	
Iv Magnesium	(-)	15 (33.3)	12 (37.5)	.7
	(+)	30 (66.7)	20 (62.5)	
Inhaled adrenaline	(-)	38 (84.4)	31 (96.9)	.13
	(+)	7 (15.6)	1 (3.1)	
Discharge/mortality	Exitus	1 (2.2)	4 (12.5)	.15
	Live	44 (97.8)	28 (87.5)	

Iv, intravenous; nc-HFOT, nasal cannula-high flow oxygen therapy; nc-NIV, nasal cannula-noninvasive ventilation.
*$P < .05$.
[#]Chi-square or Fisher's exact test.

Table 3. Logistic Regression Analysis#

	Single Variable					Multi Variable***				
Variable	**Beta**	**SE**	**Exp(B)**	**95% CI**	***P***	**Beta**	**SE**	**Exp(B)**	**95% CI**	***P***
Age (month)	0.01	0.006	1.012	0.999-1.024	.06					
Respiratory support time (day)	0.07	0.106	1.076	0.875-1.324	.48					
Peak flow (L/min)	0.10	0.08	1.112	0.942-1.311	.209					
Mean PEEP (cmH_2O)	0.60	0.471	0.546	0.217-1.373	.198					
Peak PEEP (cmH_2O)	0.268	0.376	0.765	0.366-1.598	.476					
Prism-3	0.143	0.086	1.154	0.975-1.365	.09					
Chronic illness*	1.171	0.700	5.57	1.41-21.9	**.01**	1.775	0.728	5.9	1.41-24.5	**.01**
Respiratory support type (NIV)**	1.539	0.648	4.65	1.30-16.5	**.01**	1.599	0.681	4.95	1.3-18.8	**.01**

NIV, noninvasive ventilation; PEEP, positive end-expiratory pressure; Prism-3, pediatric risk of mortality score-3.
*Nagelkerke r^2: 0.146, Cox and Snell r^2: 0.09, −2Log likelihood: 65.78.
**Nagelkerke r^2: 0.128, Cox and Snell r^2: 0.078, −2Log likelihood: 66.74.
***Nagelkerke r^2: 0.26, Cox and Snell r^2: 0.159, −2Log likelihood: 59.65.
#Hosmer–Lemeshow test.

of chronic disease in the case were identified as significant factors in terms of intubation need (Table 3). In cases where nc-NIV was chosen initially, the probability of requiring intubation was found to be 4.95 times higher than those using nc-HFOT (OR: 4.95, 95% CI: 1.3-18.8, *P* = .01). Cases with chronic diseases were found to have a 5.9 times higher probability of requiring intubation compared to those without (OR: 5.9, 95% CI: 1.41-24.5, *P* = .01).

DISCUSSION

High-flow nasal cannula oxygen therapy is known for its comfort, being less invasive, and low cost when compared to other non-invasive respiratory support methods.[11,12] Therefore, its increased usage in recent years has been shown to potentially reduce the need for intubation.[13] Besides these, studies have indicated that the risk of failure in nc-HFOT, defined as the need for intubation, varies between 8% and 19%.[14] Milési et al[15] made a comparison between nc-HFOT and CPAP and found that 50.7% of the cases treated with nc-HFOT at a flow rate of 2 L/kg/min had treatment failure, while 31% of the cases treated with 7 cmH_2O CPAP had treatment failure. The authors concluded from their study that nc-HFOT is less effective than CPAP in cases of acute viral bronchiolitis with hypercapnia. In another study, where 9 randomized controlled trials were evaluated, and standard oxygen therapy (SOT), nc-HFOT, and CPAP treatments were compared, treatment failure in the nc-HFOT group was found to be lower than in the SOT group but higher than in the CPAP group.[16] In adult studies related to ARF, while nc-HFOT has shown better results in terms of intubation compared to SOT, it has not shown better results than NIV.[17]

In our intensive care unit, nc-HFOT is a frequently performed respiratory support method. However, in cases where our 2 devices are not sufficient, or when the PICU team encounters an indication for NIV, patients are treated with NIV using the same cannulas and mechanical ventilation devices in PC mode. This method of use is common in many PICUs in our country. The reason we apply NIV with a cannula and an intensive care ventilator is both because we do not have a specific device that only provides NIV and also because we do not have suitable interfaces. Despite the increased use of NIV and various interface options in the literature, there are few studies comparing the effectiveness of different interfaces in the pediatric age group.[18,19] In this study, a comparison was made between non-invasive respiratory support methods applied in the PICU in terms of intubation, and it was found that the intubation rate was higher in the group initially treated with nc-NIV compared to the nc-HFOT group (OR: 4.95, 95% CI: 1.3-18.8, *P* = .01). An important issue related to the use of new-generation intensive care ventilators that provide NIV is that most are tolerant to air leaks.[20-22] The air leaks caused by the cannulas we use may have accelerated the need for intubation by reducing the respiratory support provided for NIV. In a study comparing nc-HFOT and non-invasive pressure support ventilation (NIPSV), it was stated that nc-HFOT provides variable pressures with a constant flow depending on the patient's respiration condition, while NIPSV provides variable flows with a constant pressure.[23] Our method of NIV, without providing clear information between the applied pressures, could not guarantee the flow as in HFOT, thus further reducing the given support treatment. In the FLORALI study, which compared SOT, nc-HFOT, and NIV, 310 patients with hypoxemic ARF were evaluated, and although there was no significant difference between the 3 groups in terms of intubation rate, it was stated that the 90-day mortality was lower in the nc-HFOT group, and this was attributed to the lower intubation rate in the sub-group consisting of severe hypoxemic patients treated with nc-HFOT (35% for SOT, 53% for nc-HFOT, and 58% for NIV, *P* = .009).[24] Although the mode we use in intensive care ventilators is PC, the fact that the applied pressures cannot provide enough tidal volume and thus cannot perform lung protection may also have contributed to our intubation event.[25,26]

The PEEP effect applied in nc-HFOT is indicated to be lower than NIV, and, therefore, the improvement in oxygenation is greater in NIV.[24,27] However, in our study, the S/F value did not differ between the groups (*P* = .12). It is reported that the S/F value in the first hour of treatment is an early and reliable predictor parameter for NIV treatment failure.[28] It has been stated that the S/F value is a better warning tool than SpO_2 or FiO_2 alone for monitoring children treated with nc-HFOT.[29] We believe that the cannulas we use, which weakly tolerate the use of high pressures, also contributed to this result.[30]

The result of our study is that the presence of chronic diseases increases the risk of intubation can be associated with the underlying comorbid condition in these cases leading to an increased need for respiratory support treatment.

The biggest limitations of the study were its being conducted in a single center and its retrospective nature. Moreover, only the values at the start of the respiratory support method for the patients were used for vital parameters, and follow-up parameters were not included. While initial PEEP values for NIV were taken into account, PEEP above values were ignored.

In conclusion, non-invasive respiratory support methods can be used in the pre-intubation period in PICUs. In this study, providing nc-HFOT has prevented intubation 4.95 times more than the nc-NIV application. In the study, the intubation rate in patients with underlying chronic diseases was found to be 5.9 times higher than those without. We suggest that studies using the same method, with more cases, and of a prospective nature to increase the use of non-invasive respiratory support methods in PICUs are needed.

Ethics Committee Approval: This study was approved by Ethics committee of İstanbul Medeniyet University, Göztepe Training and Research Hospital(approval number: 2022/0404, date: June 29, 2022).

Informed Consent: Due to the retrospective nature of the study, no consent was obtained from patients or their guardians.

Peer review: Externally peer-reviewed.

Author Contributions: Concept - Ü.K.B., E.U.B.; Design - H.S.K., U.K.B.; Supervision - A.Ö., H.S.K.; Resources - V.T., A.Ö.; Materials - E.U.B., V.T.; Data Collection and/or Processing - A.Ö., E.U.B.; Analysis and/or Interpretation - H.S.K., V.T.; Literature Search - E.U.B., U.K.B.; Writing - U.K.B., H.S.K.; Critical Review - A.Ö., U.K.B.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: This study received no funding

REFERENCES

1. Frat JP, Coudroy R, Marjanovic N, Thille AW. High-flow nasal oxygen therapy and noninvasive ventilation in the management of acute hypoxemic respiratory failure. *Ann Transl Med*. 2017;5(14):297. [CrossRef]
2. Coletti KD, Bagdure DN, Walker LK, Remy KE, Custer JW. High-flow nasal cannula utilization in pediatric critical care. *Respir Care*. 2017;62(8):1023-1029. [CrossRef]
3. Kwon JW. High-flow nasal cannula oxygen therapy in children: a clinical review. *Clin Exp Pediatr*. 2020;63(1):3-7. [CrossRef]
4. Rubin S, Ghuman A, Deakers T, Khemani R, Ross P, Newth CJ. Effort of breathing in children receiving high-flow nasal cannula. *Pediatr Crit Care Med*. 2014;15(1):1-6. [CrossRef]
5. Pham TMT, O'Malley L, Mayfield S, Martin S, Schibler A. The effect of high flow nasal cannula therapy on the work of breathing in infants with bronchiolitis. *Pediatr Pulmonol*. 2015;50(7):713-720. [CrossRef]
6. Schmid F, Olbertz DM, Ballmann M. The use of high-flow nasal cannula (HFNC) as respiratory support in neonatal and pediatric intensive care units in Germany-A nationwide survey. *Respir Med*. 2017;131:210-214. [CrossRef]
7. Fauroux B, Boffa C, Desguerre I, Estournet B, Trang H. Longterm noninvasive mechanical ventilation for children at home: a national survey. *Pediatr Pulmonol*. 2003;35(2):119-125. [CrossRef]
8. Teague WG. Non-invasive positive pressure ventilation: current status in paediatric patients. *Paediatr Respir Rev*. 2005;6(1):52-60. [CrossRef]
9. Viscusi CD, Pacheco GS. Pediatric emergency noninvasive ventilation. *Emerg Med Clin North Am*. 2018;36(2):387-400. [CrossRef]
10. Antonelli M, Conti G, Moro ML, et al. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. *Intensive Care Med*. 2001;27(11):1718-1728. [CrossRef]
11. González Martínez F, González Sánchez MI, Rodríguez Fernández R. Clinical impact of introducing ventilation with high flow oxygen in the treatment of bronchiolitis in a paediatric ward. *An Pediatr (Barc)*. 2013;78(4):210-215. [CrossRef]
12. Davison M, Watson M, Wockner L, Kinnear F. Paediatric high-flow nasal cannula therapy in children with bronchiolitis: A retrospective safety and efficacy study in a non-tertiary environment. *Emerg Med Australas*. 2017;29(2):198-203. [CrossRef]
13. Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: a literature review. *Scand J Trauma Resusc Emerg Med*. 2016;24:93. [CrossRef]
14. Brink F, Duke T, Evans J. High-flow nasal prong oxygen therapy or nasopharyngeal continuous positive airway pressure for children with moderate-to-severe respiratory distress? *Pediatr Crit Care Med*. 2013;14(7):e326-e331. [CrossRef]
15. Milési C, Essouri S, Pouyau R, et al. High flow nasal cannula (HFNC) versus nasal continuous positive airway pressure (nCPAP) for the initial respiratory management of acute viral bronchiolitis in young infants: a multicenter randomized controlled trial (TRAMONTANE study). *Intensive Care Med*. 2017;43(2):209-216. [CrossRef]
16. Lin J, Zhang Y, Xiong L, Liu S, Gong C, Dai J. High-flow nasal cannula therapy for children with bronchiolitis: a systematic review and meta-analysis. *Arch Dis Child*. 2019;104(6):564-576. [CrossRef]
17. Zhao H, Wang H, Sun F, Lyu S, An Y. High-flow nasal cannula oxygen therapy is superior to conventional oxygen therapy but not to noninvasive mechanical ventilation on intubation rate: a systematic review and meta-analysis. *Crit Care*. 2017;21(1):184. [CrossRef]
18. Hull J. The value of non-invasive ventilation. *Arch Dis Child*. 2014;99(11):1050-1054. [CrossRef]
19. Gregoretti C, Pelosi P, Chidini G, Bignamini E, Calderini E. Noninvasive ventilation in pediatric intensive care. *Minerva Pediatr*. 2010;62(5):437-458.
20. British Thoracic Society Standards of Care Committee. Non-invasive ventilation in acute respiratory failure. *Thorax*. 2002;57(3):192-211. [CrossRef]
21. Boldrini R, Fasano L, Nava S. Noninvasive mechanical ventilation. *Curr Opin Crit Care*. 2012;18(1):48-53. [CrossRef]
22. Mehta S, Hill NS. Noninvasive ventilation. *Am J Respir Crit Care Med*. 2001;163(2):540-577. [CrossRef]
23. Mas A, Masip J. Noninvasive ventilation in acute respiratory failure. *Int J Chron Obstruct Pulmon Dis*. 2014;9:837-852. [CrossRef]
24. Frat JP, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015;372(23):2185-2196. [CrossRef]
25. Carteaux G, Millán-Guilarte T, De Prost N, et al. Failure of noninvasive ventilation for de novo acute hypoxemic respiratory failure: role of tidal volume. *Crit Care Med*. 2016;44(2):282-290. [CrossRef]
26. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med*. 2014;370(10):980. [CrossRef]
27. Frat JP, Brugiere B, Ragot S, et al. Sequential application of oxygen therapy via high-flow nasal cannula and noninvasive ventilation

in acute respiratory failure: an observational pilot study. *Respir Care*. 2015;60(2):170-178. [CrossRef]
28. Mayordomo-Colunga J, Pons M, López Y, et al. Predicting non-invasive ventilation failure in children from the SpO_2/FiO_2 (SF) ratio. *Intensive Care Med*. 2013;39(6):1095-1103. [CrossRef]
29. Kamit Can F, Anil AB, Anil M, et al. Predictive factors for the outcome of high flow nasal cannula therapy in a pediatric intensive care unit: is the SpO_2/FiO_2 ratio useful? *J Crit Care*. 2018;44:436-444. [CrossRef]
30. Mortamet G, Amaddeo A, Essouri S, Renolleau S, Emeriaud G, Fauroux B. Interfaces for noninvasive ventilation in the acute setting in children. *Paediatr Respir Rev*. 2017;23:84-88. [CrossRef]