ORIGINAL ARTICLE

AHI EVRAN MEDICAL JOURNAL
E-ISSN: 2619 - 9203

Evaluation of Clinical and Epidemiological Features of Patients Receiving High-Flow Nasal Cannula Oxygen Therapy in the Pediatric Intensive Care Unit

Çocuk Yoğun Bakım Ünitesinde Yüksek Akımlı Nazal Kanül Oksijen Tedavisi Alan Hastaların Klinik ve Epidemiyolojik Özelliklerinin Değerlendirilmesi

***Osman BÜYÜKŞEN*[1] *Süleyman BAYRAKTAR*[2] *Murat ELEVLİ*[1]**

ÖZ

Amaç: Akut solunum yetmezliğinde solunum desteği yöntemlerinden biri, giderek kullanım sıklığı artan yüksek akımlı nazal kanül oksijen tedavisidir (YANKOT). Bu çalışmada, solunum yetmezliği nedeniyle çocuk yoğun bakım ünitesine yatırılan ve YANKOT uygulanan hastaların retrospektif olarak değerlendirilmesi amaçlandı.
Araçlar ve Yöntem: Çalışma retrospektif olarak, Ocak 2015- Aralık 2017 tarihleri arasında çocuk yoğun bakım ünitesinde yatan ve YANKOT uygulanmış 104 hasta alınarak yapıldı.
Bulgular: Çalışmaya katılan hastaların yaşlarının medyan değeri 5 ay olarak saptandı. En sık yatış endikasyonu %97.1 oranında alt hava yolu hastalığıydı ve hastaların %52.9'unda tip 1 solunum yetmezliği saptandı. Çocuk yoğun bakımdaki yatış süresi medyan değeri 7 gün iken, YANKOT uygulama süresi medyan değeri 48 saat olarak saptandı. YANKOT alırken entübe olan hastalarda (%28.8) kronik hastalık ve kronik akciğer hastalığı entübe olmayanlara göre belirgin olarak yüksekti (p=0.001, p=0.033, sırasıyla). Hastalarda komplikasyon olarak %8.7'sinde nazal bölgede cilt hasarı, %1.9'unda pnömotoraks geliştiği saptandı. Çocuk yoğun bakım ünitesine yatıp YANKOT alırken ölen hastalarda kronik hastalık ve konjenital kalp hastalığı oranları hayatta kalan hastalara göre belirgin olarak yüksekti (p=0.043, p=0.003, sırasıyla).
Sonuç: Son yıllarda çocuklarda solunum yetmezliği tedavisinde kullanılmaya başlanan YANKOT'un sonuçları genellikle yüz güldürücüdür. Bununla birlikte bu yeni yöntemde komplikasyonların gelişebilmesi nedeniyle uygulama süresince yakın izlem gerekmektedir.

Anahtar Kelimeler: çocuk; çocuk yoğun bakım ünitesi; solunum yetersizliği; oksijen tedavisi

ABSTRACT

Purpose: One of the respiratory supports in acute respiratory failure (ARF) is high-flow nasal cannula (HFNC) oxygen therapy, which is being increasingly used in this study. We aimed to evaluate the patients with ARF who received HFNC oxygen therapy in the pediatric intensive care unit (ICU).
Materials and Methods: The study was done retrospectively in 104 patients who were admitted to the pediatric ICU and received HFNC oxygen therapy between January 2015 and December 2017.
Results: The median age of the patients participating in the study was 5 months. The most common cause of hospitalization was lower respiratory disease (97.1%), and 52.9% of the patients had type 1 respiratory failure. The median length of stay in the pediatric ICU was 7 days, while the median duration of HFNC oxygen therapy was 48 hours. In patients who were intubated during HFNC oxygen therapy (28.8%), the proportions of having a chronic disease and chronic lung disease were significantly higher than those who were not intubated (p=0.001, p=0.033, respectively). In terms of complications, nasal skin damage (8.7%) and pneumothorax (1.9%) were developed. The proportions of chronic diseases and congenital heart disease of the patients who were admitted to pediatric ICU and died after HFNC oxygen therapy were significantly higher than the survivors (p=0.043, p=0.003, respectively).
Conclusion: The results of HFNC oxygen therapy, which is being increasingly used in the treatment of respiratory failure in children, are generally satisfactory. However, due to possible complications, close monitoring is required during the application.

Keywords: child; pediatric intensive care unit; respiratory failure; oxygen therapy

Received: 20.02.2021; Accepted: 30.07.2021

[1] Health Sciences University, Istanbul Haseki Education and Research Hospital, Department of Pediatrics, Istanbul, Turkey.
[2]Health Sciences University, Istanbul Haseki Education and Research Hospital, Pediatric Intensive Care Unit, Istanbul, Turkey.
Corresponding Author: Süleyman Bayraktar, Health Sciences University, Istanbul Haseki Education and Research Hospital, Pediatric Intensive Care Unit, Istanbul, Turkey. e-mail: bsuleyman@hotmail.com

How to cite: Büyükşen O, Bayraktar S, Elevli M. Evaluation of clinical and epidemiological features of patients receiving high-flow nasal cannula oxygen therapy in the pediatric intensive care unit. Ahi Evran Med J. 2022;6(1):7-14. DOI:10.46332/aemj.883605

INTRODUCTION

Respiratory support is a frequently used treatment method in patients being followed up in the pediatric intensive care unit (ICU). This supportive care may be needed in case of lung infections, neuromuscular disorders, cardiac problems, upper airway obstructions, trauma, or post-surgical conditions.[1, 2] Oxygen therapy can be given to critically ill patients hospitalized in pediatric ICU using different methods. High-flow nasal cannula (HFNC) oxygen therapy is a new treatment method that is being increasingly used in all age groups ranging from premature babies to adult patients in the world and our country.[3, 4]

HFNC oxygen therapy is a method of delivering heated and humidified air, containing a high concentration of oxygen, to the patient at a specific flow rate through the nasal cannula. There is no universally accepted definition of minimum flow rate that defines the term "high flow". High flow rate is defined as ≥2 L/min in newborns, while it is accepted as ≥4-6 L/min for older children.[5] By delivering the heated and humidified oxygen at a high flow rate, the airway resistance and the dead space in the nasopharyngeal passage are reduced, ensuring sufficient inspiration and better gas exchange. In addition, heating and humidifying the air helps to establish effective mucociliary activity, prevent insensible fluid loss, and avert the energy loss required to warm the air. Another advantage of HFNC oxygen therapy is the positive end-expiratory pressure (PEEP) it creates in the airways. As a result of this effect, the development of atelectasis is prevented by providing sufficient functional residual capacity. However, as the PEEP created by the system is not measurable, it has been predicted that possible complications such as pneumothorax may occur due to high pressure.[5,6]

In recent years, the use of HFNC oxygen therapy in respiratory support in children has increased rapidly, particularly in ICUs. However, there is a small number of case reports and observational studies related to the use of this new method in pediatric ICU.[1,7] Questions such as the type of respiratory failure that will benefit from the treatment, the method to be chosen according to the severity of the patient, the complications of the method and its effectiveness in the case of additional chronic disease await response. Therefore, randomized-controlled, prospective studies, including more patients, should be conducted.[7]

In this study, we aimed to evaluate the indications of HFNC oxygen therapy in pediatric ICU, to define the suitable patient profile, its effectiveness in patients with comorbidities, the necessity of intubation required during the application, the effect of the procedure on blood gas parameters, the duration of the application and the complications related to the HFNC oxygen therapy.

MATERIALS and METHODS

Patients who received HFNC oxygen therapy in the pediatric ICU of SBU Haseki Training and Research Hospital between January 1, 2015 and December 31, 2017 were included in the study. The pediatric ICU has ten beds, ten ventilators and five HFNC devices. The HFNC oxygen therapy was delivered using a high-flow respiratory system (Vapotherm®, Exeter, NH, USA). The flow rate was set to 2L/kg/min. Fraction of inspired oxygen concentration (FiO_2) was started as 100%, the oxygen saturation was kept between 92-97%, and the temperature of the given air was set as 36˚C in all patients.

Demographic data, laboratory results, and radiological images of patients were analyzed retrospectively. The study was designed as a descriptive trial. Patients' age, gender, causes of hospitalization, type of respiratory failure, history of previous chronic diseases, blood gas parameters such as pH and pCO_2, the method of oxygen delivery before and after HFNC oxygen therapy, need for invasive mechanical ventilation, duration of application, the length of stay in the pediatric ICU, complications that developed after HFNC oxygen therapy, and survival were recorded in a standardized form.

In terms of admission diagnosis, diseases such as bronchiolitis, acute asthma, and pneumonia involving the lung parenchyma were classified as lower respiratory tract diseases, and diseases causing narrowing of the upper airways such as croup (laryngotracheobronchitis) were classified as upper respiratory tract diseases. The presence of concomitant chronic disease in the patients was classified and recorded as chronic lung disease, congenital heart disease, congenital metabolic, genetic, and neurological/muscular

disorders and other diseases. The children were classified into two groups due to type of respiratory failure. Type 1 ARF (hypoxemic) is defined as a low level of oxygen with either a normal or low level of carbon dioxide. Type 2 ARF (hypercarbic) involves low oxygen with high carbon dioxide.

Since not all patients had arterial catheters, the results of capillary blood gas testing, a less invasive and more practical method for children, were determined. Therefore, PaO_2 values of blood gas samples were not evaluated. The pH and PCO_2 levels in the capillary blood gas before and four hours after the HFNC oxygen therapy were measured and recorded.

pH levels were classified as follows:

a. Below 7.25;
b. Between 7.25 - 7.35;
c. Between 7.35 - 7.45;
d. Between 7.45 - 7.55;
e. Over 7.55, and

PCO_2 values were classified as

a. Below 35 mm Hg;
b. Between 35 - 45 mm Hg;
c. Between 45 - 55 mm Hg;
d. Between 55 - 65 mm Hg;
e. Over 65 mm Hg

Exclusion Criteria of the Patients

The patients were excluded from the study, if**:**

1. The patient was delivered HFNC oxygen therapy in a place other than the pediatric ICU,
2. The patient used other oxygen delivery methods that can meet the definition of HFNC oxygen therapy (delivery of oxygen with a simple nasal cannula, application of nasal continuous positive airway pressure (CPAP),
3. The patient was intubated at admission and received HFNC oxygen therapy after extubation.

On the other hand, the patients who were intubated during HFNC oxygen therapy and those who received HFNC oxygen therapy after extubation were included in the study.

SBÜ Haseki Education and Research Hospital Clinical Research Ethics Committee approved the study with the number 01R/2018/23.01.2018.

Statistical Analysis

SPSS software (version 15.0; SPSS Inc. Chicago, IL, USA) program was used for statistical analysis. Descriptive statistics were given as numbers and percentages for categorical variables and as mean, standard deviation, median, minimum, and maximum for numerical variables. If the numerical variables were not normally distributed, independent groups were compared using the Mann-Whitney U test. Categorical variables were analyzed using Chi-square Test and McNemar-Bowker Test. The statistical significance level of alpha was taken as $p<0.05$.

RESULTS

One hundred and four patients who received HFNC oxygen therapy were included in the study. The demographic and clinical characteristics of the patients are given in Table 1.

Table 1. Demographic and clinical characteristics of children who received HFNC.

Parameters	**Mean (n=104)**
Age (month), median (min-max)	5 (1-216)
Sex, (Male), % (n)	65.4 (68)
*Diagnosis (Lower respiratory tract diseases), n (%)	101 (97.1)
Chronic diseases	
Cardiac disease, % (n)	32.3 (31)
Neurologic/ muscular disease, % (n)	25.0 (24)
Lung disease, % (n)	15.6 (15)
Inborn errors of metabolism, % (n)	4.2 (4)
Other diseases, % (n)	12.5 (12)
Genetic disease, % (n)	10.4 (10)
Type of Respiratory failure	
Type 1 (Hypoxemic) respiratory failure, % (n)	52.9 (55)
Type 2 (Hypercapnic) respiratory failure, % (n)	47.1 (49)
Oxygen delivery method before HFNC	
Mask/nebul, % (n)	95.2 (99)
Duration of HFNC (hour), median (min-max)	48 (1-576)
Length of hospitalization (day), median (min-max)	7 (2-99)
Complications	
Pneumothorax, % (n)	1.9 (2)
Nasal injury, % (n)	8.7 (9)
Outcome (Mortality), % (n)	6.7 (7)

HFNC, High flow nasal cannula; CPAP, continuous positive airway pressure. Values are expressed as n (%) and median (min-max) *More than one disease has been marked.

Sixty-eight (65.4%) of the patients were male and 36 (34.6%) were female. The median age was 5 (min.1-

max.216) months. Of 104 patients, 101 (97.1%) were diagnosed with a lower respiratory tract disease. The most common type of respiratory failure among the patients who received HFNC oxygen therapy was Type 1 (hypoxemic) ARF (52.9%). Of patients, 62.5% had at least one concomitant chronic disease. The top three chronic diseases were congenital heart diseases (29.8%), neurological and/or muscular disorders (23.1%) and chronic lung diseases (14.4%).

The most common oxygen delivery methods before HFNC oxygen therapy were a simple oxygen mask or nebulizer mask (95.2%). The median length of stay in the pediatric ICU for those who received HFNC oxygen therapy due to respiratory failure was 7 (min.2-max.99) days. The median time of HFNC oxygen therapy was 48 (min.1-max.576) hours. When we compared the pH and pCO_2 levels in the capillary blood gases taken just before and 4 hours after HFNC oxygen therapy, we found that the pCO_2 value, which was initially above 45 mm Hg, returned to normal range ($35 \leq pCO_2 \leq 45$ mm Hg) after therapy in 18 of 49 (36.7%) patients. On the other hand, pCO_2 values of 39 of 49 (79.6%) patients remained within the normal range, while the values exceeded 45 mm Hg in 8 (16.3%) patients following HFNC oxygen therapy. There was no statistically significant difference in pCO_2 changes between the two groups (p=0.075) (Table 2).

The changes in the pH value of the capillary blood gas taken at the beginning and 4 hours after the HFNC oxygen therapy are shown in Table 3.

Table 2. Progression of pCO2 values in blood gas before HFNC and after the 4th hour of HFNC.

		pCO2 (After 4 hours of HFNC)										
		pCO_2 <35		$35 \leq pCO_2 \leq 45$		$45 < pCO_2 < 55$		$55 \leq pCO_2 < 65$		$pCO_2 \geq 65$		Total
		n	%	n	%	n	%	n	%	n	%	n
pCO_2 (Before HFNC)	pCO_2 <35	3	50.0	3	50.0	0	0.0	0	0.0	0	0.0	6
	$35 \leq pCO_2 \leq 45$	2	4.1	39	79.6	6	12.0	2	4.1	0	0.0	49
	$45 < pCO_2 < 55$	0	0.0	17	48.6	16	45.7	0	0.0	2	5.7	35
	$55 \leq pCO_2 < 65$	0	0.0	1	10.0	5	50.0	3	30.0	1	10.0	10
	$pCO_2 \geq 65$	0	0.0	0	0.0	1	25.0	2	50.0	1	25.0	4

p=0.075, according to McNemar-Bowker Test HFNC, High flow nasal cannula

Table 3. Progression of pH values in blood gas before HFNC and after the 4th hour of HFNC.

		pH (After 4 hours of HFNC)								
		Ph <7.25		$7.25 \leq Ph < 7.35$		$7.35 \leq Ph \leq 7.45$		7.45<Ph≤7.55		
		n	%	n	%	n	%	n	%	Total
pH (Before HFNC)	Ph <7.25	0	0.0	2	40.0	3	60.0	0	0.0	5
	$7.25 \leq Ph < 7.35$	2	5.7	12	34.3	21	60.0	0	0.0	35
	$7.35 \leq Ph \leq 7.45$	1	1.6	8	12.7	53	84.1	1	1.6	63
	Ph>7.55	0	0.0	0	0.0	1	100	0	0.0	1

p=0.075, according to McNemar-Bowker Test HFNC, High flow nasal cannula

In 24 of 40 (60%) patients whose initial pH value was below 7.35, the pH values came within the physiological limits ($7.35 \leq pH \leq 7.45$) after HFNC oxygen therapy. However, the pH values of 53 of 63 (84.1%) patients, who were within the normal range at the beginning, remained within limits, while pH decreased below 7.35 in 9 (14.3%) patients. There was no statistically significant difference between the two groups in terms of pH changes (p=0.075).

While 30 (28.8%) of the patients needed invasive mechanical ventilation during HFNC oxygen therapy, 64 (70.2%) of the patients showed clinical improvement and their treatment was continued with a simple oxygen mask. In our study, 21.8% of the patients with Type 1 (hypoxemic) ARF and 36.7% of the patients with Type 2 (hypercapnic) ARF were intubated, as they were unable to tolerate HFNC oxygen therapy. The length of hospitalization showed no significant difference between patients with Type 1 ARF and Type 2 ARF (p>0.05).

Of these 30 patients who were intubated during HFNC oxygen therapy, 4 (13%) were extubated and kept on receiving HFNC; however, out of necessity, they had to be re-intubated. Unfortunately, 23.3% (7) of the intubated patients died. We also examined the situations related to intubation during the HFNC oxygen therapy. In patients who were intubated during HFNC oxygen therapy, the proportions of having a chronic disease and chronic lung disease were significantly higher than those who were not intubated (p=0.001, p=0.033, respectively) (Table 4).

Table 4. Comparison of children's outcome due to intubation.

Parameters		**Intubation**				
		Yes		No		p
Length of HFNC (hour), Mean±SD (min-max)		31.6±32.1 (1-144)		92.7±105.6 (10-576)		<0.001
Length of hospitalization (day) Mean.±SD (min-max)		16.7±10.7 (3-40)		10.4±15.0 (2-99)		<0.001
		n	%	n	%	p
		26	86.7	39	52.7	0.001
	Lung disease	8	26.7	7	9.5	0.033
	Cardiac disease	11	36.7	20	27.0	0.330
***Chronic diseases**	Neurologic/ muscular disease	10	33.3	14	18.9	0.114
	IEM	2	6.7	2	2.7	0.577
	Genetic disease	4	13.3	6	8.1	0.469
	Other diseases	4	13.3	8	10.8	0.740
Diagnosis at admission	Upper airway disease	0	0.0	3	4.1	0.555
	Lower airway disease	30	100	71	95.9	
Type of respiratory failure	Type 1 (hypoxemic)	5	16.7	25	33.8	0.081
	Type 2 (hypercapnic)	25	83.3	49	66.2	

Values are mean (SD) or n (%) and (min-max) HFNC, High flow nasal cannula; IEM, Inborn errors of metabolism
*More than one disease has been marked

Table 5. Evaluation of the factors that affected the survival in patients received HFNC

Parameters		**Outcome**				
		Alive		Mortality		p
Length of HFNC Mean±SD (min-max)		78.2±97.1 (1-576)		31.1±25.1 (2-62)		0.083
Length of hospitalization Mean ±SD (min-max)		12.7±14.6 (2-99)		5.9±3.0 (3-11)		0.182
		n	%	n	%	
Chronic disease		58	59.8	7	100.0	0.043
	Lung disease	14	14.4	1	14.3	0.999
	Cardiac disease	25	25.8	6	85.7	0.003
	Neurologic/muscular disease	23	23.7	1	14.3	0.999
	IEM	3	3.1	1	14.3	0.246
	Genetic disease	9	9.3	1	14.3	0.518
	Other diseases	12	12.4	0	0.0	0.999
Diagnosis at admission	Upper respiratory disease	3	3.1	0	0.0	0.999
	Lower respiratory disease	94	96.9	7	100.0	
Type of respiratory failure	Type 1 (hypoxemic)	29	29.9	1	14.3	0.670
	Type 2 (hypercapnic)	68	70.1	6	85.7	
Oxygen therapy before HFNC	None	5	5.2	0	0.0	0.999
	Nebul-face mask	92	94.8	7	100.0	
pH (Before HFNC)	Ph <7.25	4	4.1	1	14.3	0.328
	$7.25 \leq Ph < 7.35$	32	33.0	3	42.9	
	$7.35 \leq Ph \leq 7.45$	60	61.9	3	42.9	
	Ph>7.55	1	1.0	0	0.0	
PCO_2 (Before HFNC)	PCO_2 <35	6	6.2	0	0.0	0.426
	$35 \leq PCO_2 \leq 45$	46	47.4	3	42.9	
	$45 < PCO_2 < 55$	33	34.0	2	28.6	
	$55 \leq PCO_2 < 65$	9	9.3	1	14.3	
	$PCO_2 \geq 65$	3	3.1	1	14.3	
Complications	Pneumothorax	2	2.1	0	0.0	0.999
	Nasal injury	9	9.3	0	0.0	

Values are mean (SD) or n (%) and (min-max) HFNC, High flow nasal cannula

When we investigated the complications that developed during HFNC oxygen therapy, we found that 93 (89.4%) of the patients did not develop any complications, while 9 (8.7%) had skin damage in the nasal area, and 2 (1.9%) had pneumothorax.

The proportions of chronic diseases and congenital heart disease of the patients who were admitted to pediatric ICU and died after HFNC oxygen therapy were significantly higher than the survivors (p=0.043, p=0.003, respectively) (Table 5). Among all patients, 6.7% of them died after being admitted to the pediatric ICU.

DISCUSSION

In this retrospective descriptive study, we found that HFNC oxygen therapy has been widely used in type 2 ARF as often as type 1 ARF. One of the most important steps in the treatment approach to ARF is oxygen therapy. Oxygen delivered under appropriate conditions and with proper methods not only accelerates the healing process of the disease but also reduces mortality and morbidity by preventing the worsening of the current situation.[8]

Recently, many invasive and non-invasive methods have been developed regarding the method of oxygen delivery. Non-invasive methods are preferred as much as possible because invasive methods extend the duration of hospital stay and are more susceptible to the development of complications.[1,9] It has been emphasized that in order to get the most benefit from the oxygen to be delivered, it should be humidified, heated and given the concentration that the patient required.[5,10,11] In addition, considering that the flow rate of the supplied air can also increase the efficacy of the treatment, high-flow oxygen delivery methods have been developed.[1,7]

HFNC oxygen therapy is an oxygen delivery method that is being increasingly used in various age groups and in inpatient pediatric wards, emergency departments and ICUs.[3,4] Even though it is frequently used, the number of studies investigating its indications, efficacy and safety has not reached the desired level yet. In our study, HFNC oxygen therapy was used in all pediatric age groups ranging between 1-216 months who were admitted to the pediatric ICU. It has been shown that HFNC oxygen therapy can be used effectively in children with pneumonia, bronchiolitis, asthma, cardiogenic and pulmonary edema.[7,12,13] Most of our patients had lower respiratory tract infections, depending on the unit where the study was conducted. If the study was planned in the emergency department, upper respiratory tract infections might be the leading disease. It has been reported that the HFNC oxygen therapy can increase the success proportion of treatment for ARF, especially if it is given in the early period.[3,14] Although some studies have shown its benefits after extubation, exacerbation of chronic respiratory failure, and Type 1 (hypoxemic) respiratory failure, the studies on the efficacy of HFNC oxygen therapy in children with ARF is limited.[15] Our study group consisted of both Type 1 and Type 2 ARF. There were studies on the use of HFNC oxygen therapy in cases of hypoxemic (Type 1) ARF.[1,6,7] HFNC oxygen therapy has been shown favorable benefits in adults, though there was no strong evidence about the utility of HFNC for type 1 ARF in children.[16] The results of our study also showed that HFNC could be beneficial in the cases of hypercapnic (Type 2) ARF in children. Accordingly, prospective, randomized-controlled trials which will investigate the efficacy of HFNC oxygen therapy on Type 2 ARF and concomitant diseases in pediatric patients are needed.[17]

Studies have shown that HFNC oxygen therapy reduces the need for intubation by 8-19% in patients with ARF.[17,18]. Another study has reported the proportion of intubation as 20% in patients who received HFNC oxygen therapy due to ARF.[15] The patients with Type 1 and Type 2 ARF have been shown no significant difference according to intubation proportions and length of hospitalization in our study. A study of adult patients with hypoxemic respiratory failure found higher partial pressure of oxygen (PO2) concentrations when managed with HFNC compared with oxygen delivery using a face mask.[19] At this point, close monitoring seems an essential component of the proper use of HFNC.

It has been reported that 78.7% of patients, who underwent non-invasive ventilation, had a concomitant chronic disease, and the most common comorbidities were chronic neurological, neuromuscular and congenital metabolic disorders and congenital heart diseases.[9] In a study of Yurtseven and Saz, 53% of patients had chronic diseases,

and the most common one was neuromuscular disease. We also found similar proportions in our study, except cardiac diseases were in the first place. They reported that there were not statistical differences between patients, who have a chronic disease or not, in treatment failure and intubation proportion.[20] Unlike their study, we demonstrated that in patients who were intubated due to failure of HFNC oxygen therapy, chronic lung disease was the most common. Therefore, we can suggest that one should not be insistent on HFNC oxygen therapy in children with chronic lung disease and that non-invasive or invasive mechanical ventilation should be started earlier.

Blood gas monitoring is considered to be one of the most important parameters in the assessment of respiratory support, especially in evaluating the efficacy of the administered oxygen. Baudin et al.[21] mentioned that HFNC improved pH and PCO2 levels in children aged between 1-18 years old. Oto et al.[15] have used HFNC oxygen therapy in 50 patients admitted to the pediatric ICU due to hypoxemic ARF. They have shown that the treatment has significantly decreased the heart and respiratory rates of the patients. The levels of sPO_2 have decreased between the baseline and 30-minute, but they have remained similar between the 30th minute and the 12th hour.[15] They have not reported any significant changes in pH, $PaCO_2$, paO_2, SBP, and DBP values of the patients.[15] Testa et al.[17] have compared the conventional oxygen therapy with HFNC oxygen therapy in a group of 89 pediatric patients that underwent cardiac surgery, and they have reported that there was no difference between the two groups in terms of $PaCO_2$ values and re-intubation rates, while PaO_2 values were higher in the HFNC oxygen therapy group. In our study, we showed that the patients whose pCO_2 values were closer to the physiological limit returned to normal more frequently after the HFNC oxygen therapy. Even though there was no statistically significant difference, we found that pH values were improved after HFNC oxygen therapy. Prospective studies involving a larger number of patients may help classify patients according to their age and chronic disease so that blood gas parameters can be used to determine which patients will benefit from treatment.

In studies showing the beneficial effects of HFNC oxygen therapy, the complications have not been mentioned adequately. Capan et al.[18] have reported a case of pneumothorax who received HFNC oxygen therapy due to respiratory failure. Hegde et al.[22] have published three cases in which pneumothorax and pneumomediastinum developed, and one patient was lost during HFNC oxygen therapy. Koksoy et al.[9] have reported a case of pneumothorax in one of fourteen patients who received HFNC oxygen therapy. Inappropriate use of nasal cannula, inadequate sedation, and patient's adaptation problems have been suggested as the causes of these complications.[9,18,22] Another study has reported that, when compared to nasal CPAP, HFNC oxygen therapy did not make a significant difference in terms of complications such as treatment failure, pneumothorax, intraventricular bleeding, and acidosis.[23] In our study, we detected pneumothorax and skin damage in the nasal area in a few patients. None of the patients died due to complications of HFNC oxygen therapy. Close monitoring in ICU and early intervention (e.g., intubation and chest tube) before clinical deterioration may have prevented death due to complications, such as pneumothorax. Lin et al.[24] reported that there had been no differences in length of hospitalization, duration of oxygen therapy, intubation rate, and adverse events between children who received HFNC or other oxygen therapies. Another study showed that using HFNC oxygen therapy has increased the pediatric ICU stay.[25] In our study the length of pediatric ICU stay was widely distributed due to the characteristics of the patients.

Mortality is higher in patients with metabolic acidosis (pH<7.25) and hypercarbia ($PaCO_2$> 65 mmHg). This suggests that other invasive and non-invasive respiratory support methods should be considered primarily in patients with significant acidosis and high $PaCO_2$ values instead of HFNC.

There were some limitations in this study. This was a small retrospective, descriptive study that evaluated the data of patients who received HFNC oxygen therapy in our pediatric ICU only in the past two years. Due to the study nature, we could not compare the HFNC oxygen therapy with other therapy options.

The results of HFNC oxygen therapy, which is being increasingly used in the treatment of ARF in children, are generally satisfactory. However, due to possible complications of nasal skin damage and pneumothorax, close monitoring is required during the application. Further trials might focus on the development and validation of models with traits predicting success or failure of HFNC in children, aiding earlier recognition of those likely to succeed or require invasive ventilation.

Conflict of Interests

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Authors' Contributions

Concept/Design: OB, SB, ME. Data Collection and/or Processing: OB, SB. Data analysis and interpretation: OB, SB, ME. Literature Search: OB, SB. Drafting manuscript: OB, SB. Critical revision of the manuscript: OB, SB, ME. Supervision: OB, SB, ME.

REFERENCES

1. Mayfield S, Jauncey-Cooke J, Hough JL, Schibler A, Gibbons K, Bogossian F. High-flow nasal cannula therapy for respiratory support in children. Cochrane Database Syst Rev. 2014;2014(3):CD009850.
2. Söğütlü Y, Biçer S, Kurt G, ve ark. Alt solunum yolu hastalığı olan çocuklarda yüksek akımlı nazal kanül oksijenasyon tedavisinin yaşamsal bulgular üzerindeki sonuçları. J Pediatr Emerg Intensive Care Med. 2016;3(3):121-130.
3. Wing R, James C, Maranda LS, Armsby CC. Use of high-flow nasal cannula support in the emergency department reduces the need for intubation in pediatric acute respiratory insufficiency. Pediatr Emerg Care. 2012;28(11):1117-1123.
4. Lee JH, Rehder KJ, Williford L, Cheifetz IM, Turner DA. Use of high flow nasal cannula in critically ill infants, children, and adults: a critical review of the literature. Intensive Care Med. 2013;39(2):247-257.
5. Slain KN, Shein SL, Rotta AT. The use of high-flow nasal cannula in the pediatric emergency department. J Pediatr (Rio J). 2017;93(1):36-45.
6. Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: a literature review. Scand J Trauma Resusc Emerg Med. 2016;24(1):1-12.
7. Kezer S, Eryavuz Ö, Okuyan H. E, Atakan S. K, Mutlu D, Demirkol D. solunum yetersizliğinde yüksek akımlı oksijen tedavisi. Pediatri. 2018;10(3):12-18.
8. Friedman ML, Nitu ME. Acute respiratory failure in children. Pediatr Ann. 2018;47(7):e268-e273.
9. Köksoy ÖT, Paksu MŞ, Yener N, Kaplan EM. Çocuk yoğun bakım ünitesinde invaziv olmayan mekanik ventilasyon uygulanan hastaların geriye dönük değerlendirilmesi. J Pediatr Emerg Intensive Care Med. 2016;3(2):62-68.
10. Hasani A, Chapman TH, McCool D, Smith RE, Dilworth JP, Agnew JE. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. Chron Respir Dis. 2008;5(2):81-86.
11. Rea H, McAuley S, Jayaram L, et al. The clinical utility of long-term humidification therapy in chronic airway disease. Respir Med. 2010;104 (4):525-533.
12. Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: mechanisms of action. Respir Med. 2009;103(10):1400-1405.
13. Masip J, Roque M, Sánchez B, Fernández R, Subirana M, Expósito JA. Noninvasive ventilation in acute cardiogenic pulmonary edema:systematic review and meta-analysis. JAMA. 2005;294(24):3124-3130.
14. Milési C, Boubal M, Jacquot A, et al. High-flow nasal cannula: recommendations for daily practice in pediatrics. Ann Intensive Care. 2014;4(1):1-7.
15. Oto A, Erdogan S, Bosnak M. Oxygen therapy via high flow nasal cannula in pediatric intensive care unit. Turk J Pediatr. 2016;58(4):377-382.
16. Roca O, Riera J, Torres F, Masclans JR. High-flow oxygen therapy in acute respiratory failure. Respir Care. 2010;55(4):408-413.
17. Testa G, Iodice F, Ricci Z, et al. Comparative evaluation of high-flow nasal cannula and conventional oxygen therapy in paediatric cardiac surgical patients: a randomized controlled trial. Interact Cardiovasc Thorac Surg. 2014;19(3):456-461.
18. Çapan K, Apaydın HO, Geyik M. Yüksek akımlı nazal kanül oksijenasyon tedavisine bağlı pnömotoraks olgusu. J Pediatr Emerg Intensive Care Med. 2017;4(2):80-83.
19. Schwabbauer N, Berg B, Blumenstock G, Haap M, Hetzel J, Riessen R. Nasal high-flow oxygen therapy in patients with hypoxic respiratory failure: effect on functional and subjective respiratory parameters compared to conventional oxygen therapy and non-invasive ventilation (NIV). BMC Anesthesiol. 2014;14(1):1-7.
20. Yurtseven A, Saz EU. The effectiveness of heated humidified high-flow nasal cannula in children with severe bacterial pneumonia in the emergency department. J Pediatr Res. 2020;7(1):1-7.
21. Baudin F, Buisson A, Vanel B, Massenavette B, Pouyau R, Javouhey E. Nasal high flow in management of children with status asthmaticus: a retrospective observational study. Ann Intensive Care. 2017;7(1):1-9.
22. Hegde S, Prodhan P. Serious air leak syndrome complicating high-flow nasal cannula therapy: a report of 3 cases. Pediatrics. 2013;131(3):e939-e944.
23. Fleeman N, Mahon J, Bates V, et al. The clinical effectiveness and cost-effectiveness of heated humidified highflow nasal cannula compared with usual care for preterm infants: systematic review and economic evaluation. Health Technol Assess. 2016;20(30):1-68.
24. 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.
25. Kawaguchi A, Yasui Y, deCaen A, Garros D. The clinical ımpact of heated humidified high-flow nasal cannula on pediatric respiratory distress. Pediatr Crit Care Med. 2017;18(2):112-119.