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HFNC EXPERIENCE IN A NEWLY ESTABLISHED PEDIATRIC INTENSIVE CARE UNIT IN EASTERN ANATOLIA

Doğu Anadolu'da Yeni Kurulan Bir Çocuk Bakım Ünitesinde HFNC Deneyimi

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ABSTRACT

High-flow nasal cannula oxygen therapy (HFNC) is increasingly used in the treatment of acute respiratory failure. It has important effects in patients with respiratory distress. In our study, we planned to share our HFNC experiences in our newly established pediatric intensive care unit. All children between the ages of 1 month and 18 years were included in this retrospective study. Of the 126 patients, 74 (58.7%) were male. The mean age was 59.8±66.7 months. Significant differences were observed between the heart rate, oxygen saturation and respiratory rate of the patients before treatment and at the 1st, 8th and 24th hours after treatment. 16 (12.7%) of the patients were intubated due to HFNC failure. The SpO2/FiO2 ratio at presentation of those who were intubated was found to be significantly lower than the value of those who were not intubated ($p<0.001$). The admission HFNC FiO2 value, intensive care unit stay and hospital stay of intubated patients were found to be significantly higher than the values of non-intubated patients ($p<0.001$). We believe that HFNC can be used successfully in pediatric intensive care units for various etiologies of acute respiratory distress, paying attention to treatment failure and possible complications.

Keywords: High flow nasal cannula oxygen therapy, Intensive care, Pediatric.

ÖZ

Yüksek akışlı nazal kanül oksijen tedavisi (HFNC), akut solunum yetmezliği tedavisinde gün geçtikçe daha sık kullanılmaktadır. Solunum sıkıntısı olan hastalarda önemli etkileri mevcuttur. Çalışmamızda, yeni kurulan çocuk yoğun bakım ünitemizdeki HFNC deneyimlerimizi paylaşmayı planladık. Bu retrospektif çalışmaya 1 ay 18 yaş arası tüm çocuklar dahil edildi. Toplam 126 hastanın 74'ü (%58,7) erkekti. Ortalama yaş 59,8±66,7 ay idi. Hastaların tedavi öncesi, tedavi sonrası 1.saat, 8.saat ve 24.saatteki kalp atım sayıları, oksijen saturasyonları ve solunum sayıları arasında istatistiksel olarak anlamlı farklılık görüldü. Hastaların 16'sı (%12,7) HFNC başarısızlığı sonucu entübe edildi. Entübe edilenlerin başvurudaki SpO_2/FiO_2 oranı entübe edilmeyenlerin değerinden anlamlı şekilde düşük bulundu ($p<0,001$). Entübe edilen hastaların başvuru HFNC FiO_2 değeri, yoğun bakım yatış süresi ve hastanede yatma süresi entübe edilmeyenlerin değerlerinden anlamlı şekilde yüksek saptandı ($p<0,001$). Tedavi başarısızlığına ve olası komplikasyonlara dikkat edilerek HFNC'nin çocuk yoğun bakım ünitelerinde çeşitli akut solunum sıkıntısı etiyolojilerinde başarılı bir şekilde kullanılabileceğini düşünüyoruz.

Anahtar kelimeler: Çocuk, Yoğun bakım, Yüksek akışlı nazal kanül oksijen tedavisi.

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INTRODUCTION

Acute respiratory distress is one of the most common reasons for admission to the pediatric emergency department and hospitalization in the pediatric intensive care unit (PICU). Invasive and noninvasive mechanical ventilation (MV) applications are used in patients with signs of respiratory failure (Khemani et al., 2019). Invasive MV is an effective respiratory support method used in acute respiratory distress. However, in addition to its effectiveness, it also carries side effects such as nosocomial infection, sedation-related complications and prolonged intensive care unit stays. Due to these disadvantages associated with invasive MV and the high risk of complications, noninvasive MV methods have become more preferred (Mas & Masip, 2014).

High flow nasal cannula (HFNC) oxygen therapy is a noninvasive method of respiratory support that has gained prominence in recent years and is being used with increasing frequency in the treatment of respiratory failure. With HFNC, heated and humidified oxygen is administered at high flows and concentrations, resulting in a reduction in anatomical dead space and a continuous expiratory positive airway pressure (Kwon, 2020). It is widely used in pediatric and adult emergency departments and intensive care units (Mitsuyama, Nakao, Shimazaki, Ogura & Shimazu , 2022). In the pediatric age group, the most common use of HFNC is bronchiolitis in infants under 2 years of age, and it has been shown to reduce respiratory distress and intubation rates in these patients, to be more comfortable and well tolerated compared to conventional oxygen delivery methods, and to shorten the length of stay in PICUs (Dafydd, Saunders , Kotecha & Edwards, 2021).

The use of HFNC has also come to the fore during the COVID-19 pandemic. At the beginning of the pandemic, there were concerns about its use due to the fact that it was an aerosol-forming procedure and caused an increase in the risk of transmission. However, as the pandemic progressed, HFNC was shown to be superior to traditional oxygen delivery methods and to cause a decrease in intubation rates and intensive care unit length of stay (Gürün et al., 2020).

Although there are studies in the literature on the use of HFNC as respiratory support in infants with bronchiolitis in general, there are fewer studies investigating the disease state requiring HFNC treatment in older children in PICUs (Nolasco , Manti, Leonardi, Vancheri & Spicuzza, 2022).

In this study, we wanted to share our experiences with HFNC in a resource limited tertiary PICU which established at the beginning of the COVID-19 pandemic in the Eastern Anatolia region of Turkey.

MATERIAL AND METHOD

Study design, setting

This retrospective study was conducted in the tertiary PICU of Malatya Training and Research Hospital between September 1, 2020 and April 1, 2022. Clinical Research Ethics Committee approval was obtained from Malatya Turgut Ozal University for the study (Date:26.07.2023, Number: B.197). This study was conducted in accordance with the Declaration of Helsinki. Informed consent was waived because of the retrospective nature of the study.

Participants

All children aged 1 month to 18 years who underwent HFNC in the 6-bed medical-surgical PICU with an annual average of 500 patient admissions were included in the study. Treatment was performed with ‘Fisher and Paykel Healthcare (Optiflow, Auckland, New Zeland)’, the only HFNC device available in the hospital. The decision of HFNC application, daily weaning decision or transition to invasive mechanical ventilation with treatment failure was made by a team of pediatric intensivist and pediatricians.,

Measurements

Demographic characteristics, underlying disease status, HFNC indication, oxygen saturation/fraction of inspired oxygen (SpO_2/FiO_2) at admission, HFNC flow at admission, maximum HFNC flow, HFNC FiO_2 at admission, heart rate, respiratory rate and oxygen saturation level at 1 hour, 8 hours and 24 hours, duration of HFNC application, intubation as a result of HFNC failure, the duration of intensive care unit stay and hospitalization were obtained from hospital records and retrospectively recorded. The need for invasive mechanical ventilation was defined as HFNC failure.

Statistical Analysis

The analyses were evaluated in SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) 22 package program. Descriptive data were presented as n, % values for categorical data and mean±standard deviation and median (minimum-maximum) values for continuous data. Chi-square analysis (Pearson Chi-square) was used to compare categorical variables between groups. Compliance of continuous variables with normal distribution was evaluated by Kolmogorov-Smirnov Test. Mann-Whitney U test was used to compare the measured data between two groups. Friedman test was applied for repeated deaths. Receiver operating characteristic (ROC) curves were drawn to measure the diagnostic value of the initial SpO_2/FiO_2 value. Statistical significance level was accepted as $p<0.05$ in the analyses.

RESULT

Seventy-four (58.7%) of the total 126 patients were male. The mean age was 59.8±66.7 months. An underlying disease (neurological, hematological, respiratory) was present in 33 patients (26.1%). Indications for HFNC were pneumonia (56.2%), bronchiolitis (30.1%), asthma (4%), sepsis (4%), post-extubation (5.6%) in Table 1. Twenty-one (29.5%) of the patients with pneumonia were patients who underwent HFNC for COVID-19 pneumonia.

Table-1. General Demographic Characteristics of The Patients

		Total
		n (%)
Age		59.8±66.7 25.5 (2-214)
PRISM III score		7.76±3.49
Gender	Woman	52 (41.3)
	Man	74 (58.7)
Underlying disease	Healthy	93 (73.8)
	Neurological	14 (11.1)
	Asthma	11 (8.7)
	Hematological	8 (6.3)
HFNC indication	Pneumonia	71 (56.3)
	Bronchiolitis	38 (30.1)
	Asthma	5 (4.0)
	Sepsis	5 (4.0)
	Post-extubation	7 (5.6)

*Chi-square analysis,
**Mann Whitney U test were performed.

Sixteen (12.7%) of the patients were intubated as a result of HFNC failure. It was determined that 50% of patients with neurological disease, 37.5% of patients with hematological disease and 6.4% of previously healthy patients were intubated in Table 2. Among patients with COVID-19 pneumonia, 19% were intubated due to HFNC failure.

Table 2. Comparison of Patients' Demographic Characteristics with HFNC Failure Status

	Intubated (n=16)	**Non-intubated (n=110)**	**Total**	**p***
	n (%)	n (%)	n (%)	
Age	81.1±71.8 77.5 (6-197)	56.7±65.7 24.5 (2-214)	59.8±66.7 25.5 (2-214)	0.283**
PRISM III score	9.36±3.7	7.53±3.4	7.76±3,49	0.103

Gender	Female	5 (9.6)	47 (90.4)	52 (41.3)	0.384
	Male	11 (14.9)	63 (85.1)	74 (58.7)	
Underlying disease	Healthy	6 (6.4)	87 (93.6)	93 (73.8)	<0.001
	Neurological	7 (50.0)	7 (50.0)	14 (11.1)	
	Asthma	0 (0)	11 (100.0)	11 (8.7)	
	Hematological	3 (37.5)	5 (62.5)	8 (6.3)	
HFNC indication	Pneumonia	11 (15.5)	60 (84.5)	71 (56.3)	0.002
	Bronchiolitis	0 (0)	38 (100.0)	38 (30.1)	
	Asthma	0 (0)	5 (100.0)	5 (4.0)	
	Sepsis	2 (40.0)	3 (60.0)	5 (4.0)	
	Post-extubation	3 (42.9)	4 (57.1)	7 (5.6)	

The admission SpO_2/FiO_2 ratio of intubated patients was significantly lower than non-intubated patients (p<0.001). The admission HFNC FiO_2 value, length of stay in PICU and hospital of intubated patients were significantly higher than non-intubated patients (p<0.001) in Table 3.

Table 3. Comparison of Various Parameters of Patients According to Intubation Status

	Intubated (n=16)	**Non-intubated (n=110)**	**Total**	
	Mean±SD **Median (min-max)**	**Mean±SD** **Median (min-max)**	**Mean±SD** **Median (min-max)**	**p***
Admission HFNC FiO_2	77.2±8.9 80.0 (50.0-85.0)	51.7±6.4 50.0 (45.0-70.0)	55.0±10,9 50.0 (45.0-85.0)	<0.001
Admission SpO_2/ FiO_2 ratio	170.3±30.1 176.0 (120.0-234.0)	223.9±17.2 224.0 (153.0-288.0)	217.1±26.2 224.0 (120,0-288,0)	<0.001
Admission HFNC flow	25.3±10.1 25.0 (12.0-50.0)	22.5±9.2 2.0 (8.0-55.0)	22.8±9.3 20,0 (8.0-55.0)	0.240
Maximum HFNC flow	26.2±11.8 25.0 (12.0-60.0)	24.3±11.0 20.0 (10.0-80.0)	24.6±11.1 20.0 (10.0-80.0)	0.381
Duration of HFNC application	35.1±39.9 13.0 (1.0-120.0)	95.7±55.8 85.5 (18.0-312.0)	88.0±57.6 80.0 (1.0-312.0)	<0.001
Duration of intensive care hospitalization	44.9±44.8 36.0 (5.0-153.0)	6.3±4.5 5.0 (2.0-26.0)	11.2±20.6 5.0 (2.0-153.0)	<0.001
Duration of hospitalization	45.5±46.1 36.0 (5.0-157.0)	8.7±4.8 8.0 (2.0-26.0)	13.4±20.7 9.0 (2.0-157.0)	<0.001

*Mann Whitney U test was performed.

A statistically significant difference was found between the heart rate, respiratory rate and SpO_2 levels of the patients before and 1 hour, 8 hours and 24 hours after treatment (p<0.001) in Table 4, Figure1.

Table 4. Evaluation of Vital Signs of All Patients Before and During Treatment

	Heart rate	**Oxygen saturation**	**Respiratory rate**
Before treatment	139.2±30.8 144.0 (52.0-200.0)	92.0±5.9 92.0 (60.0-100.0)	38.3±13.5 36.0 (17.0-78.0)
1 hour after treatment	131.6±28.0 135.0 (48.0-189.0)	97.4±2.3 98.0 (85.0-100.0)	33.8±10.0 32.0 (16.0-60.0)
8 hours after treatment	117.8±26.5 123.5 (41.0-171.0)	98.3±1.6 99.0 (91.0-100.0)	29.6±8.1 29.0 (15.0-52.0)
24 hours after treatment	111.5±26.1 116.0 (42.0-170.0)	98.6±1.4 99.0 (88.0-100.0)	27.9±8.8 26.0 (16.0-90.0)
p*	<0.001	<0.001	<0.001

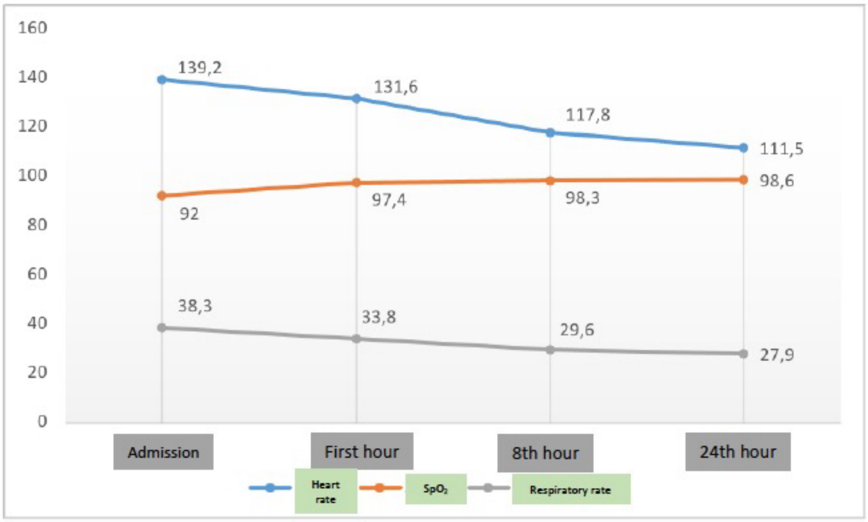

Figure 1. Heart Rate, Spo_2 and Respiratory Rate at Admission, First Hour, 8 Hours and 24 Hours After Treatment

According to the ROC analysis performed on the SpO_2/FiO_2 value according to intubation status, the cut-off point of the SpO_2/FiO_2 value was 187 (sensitivity 87.5%, specificity 97.3%). The area under the curve in the ROC curve was 0.930 in Table 5, Figure 2.

Table 5. ROC Analysis Result of Spo_2/Fio_2 Value According to Intubation Status

	SpO_2/FiO_2	**HFNC flow**	**Max. HFNC**	**Heart rate**	**SD**	**Oxygen saturation**
Cut-off point	≤187	>22	>22	≤148	≤38	>93
Responsiveness	%87.5	%62.5	%68.7	%75	%75	%56.3
Specificity	%97.3	%60.0	%55.5	%42.7	%41.8	%59.1
AUC	0.930	0.590	0.567	0.569	0.539	0.533
AUC %95	0.870-0.968	0.499-0.677	0.476-0.655	0.478-0.657	0.448-0.628	0.442-0.622
AUC p value	<0.001	0.265	0.417	0.374	0.567	0.703

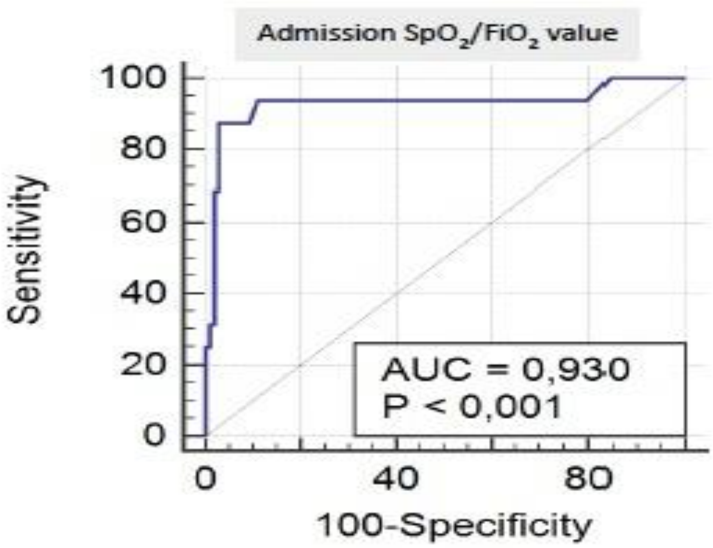

Figure 2. ROC Analysis on Spo_2/Fio_2 Value According to Intubation Status

As a complication, pneumomediastinum developed in 1 patient and pneumothorax developed in 1 other patient while under HFNC treatment. In both patients, no intervention was needed, HFNC was terminated and conventional oxygen therapy was started with a reservoir mask and the air leaks resorbed spontaneously.

DISCUSSION

The mechanism of HFNC is to reduce anatomical dead space with carbon dioxide wash-out, increase secretion clearance and excretion, reduce atelectatic areas, decrease inspiratory resistance, increase pulmonary compliance and decrease respiratory workload (Nolasco et al., 2022)

There are numerous studies recommending the use of HFNC in pediatric patients with respiratory distress and reporting good clinical course and beneficial outcomes (Esteban-Zubero et al., 2022). In this study, we wanted to share our experience with HFNC in our tertiary PICU, which was opened at the beginning of the pandemic.

There are many studies on the use of HFNC, especially in infants with bronchiolitis, and its comparison with nasal CPAP and conventional oxygen delivery methods. In a prospective, multicenter, randomized controlled study of 1472 infants with bronchiolitis, the failure rate of HFNC was found to be significantly lower compared to conventional oxygen delivery methods (Franklin et al., 2018). In another study, patients with bronchiolitis under 2 years of age who were followed up in the PICU before and after HFNC administration were evaluated and it was reported that intubation rates decreased from 23% to 9% in the post-HFNC period compared to the pre-HFNC period. According to the results of the same study, the duration of hospitalization decreased from 6 days to 4 days during the period of HFNC (McKiernan, Chua, Visintainer, Allen, 2010). In another study, only 6 (4%) of 167 patients with a primary diagnosis of viral bronchiolitis who underwent HFNC required invasive ventilation. The authors reported that HFNC reduced the need for intubation in infants with viral bronchiolitis (Schibler et al., 2011). Another study comparing HFNC with noninvasive ventilation methods (BIPAP and CPAP) evaluated 137 infants with bronchiolitis and reported a higher failure rate of HFNC compared to noninvasive ventilation methods (Habra, Janahi, Dauleh, Chandra & Veten, 2020). In a multicenter study of 17.643 bronchiolitis patients in Canada, intubation rates of clinics before and after HFNC use were compared. According to the results of this large series, it was reported that there was no decrease in intubation rates after HFNC (Garland, Gunz , Miller , Lim, 2020). In our study, 16 patients (12.7%) were intubated as a result of HFNC failure.

The use of HFNC in the post-extubation period is also common. When we look at the literature, in a study evaluating the results of conventional oxygen delivery methods and HFNC in the post-extubation period, the re-intubation rate was reported to be 22% in the group extubated with conventional oxygen and 4% in the group extubated with HFNC (Akyıldız, Öztürk, Ülgen-Tekerek, Doğanay & Görkem, 2018). Byerly et al. reported an acute and dramatic improvement with HFNC in a case intubated for inhalation burn and re-intubated due to severe inspiratory stridor after extubation (Byerly et al., 2006). In reviews including large randomized controlled trials on the use of post-extubation HFNC, it has been reported that the use of HFNC in the post-extubation period, especially in critically ill patients, improves oxygenation, reduces respiratory rate, respiratory workforce and extubation failure (Huang et al., 2018; Zhu, Yin, Zhang, Ye & Wei, 2019). There is a prospective study in adults involving 222 patients with sepsis and comparing non-invasive ventilation and HFNC in terms of preventing re-intubation in the postextubation period. According to the results of study, there was no difference between HFNC and NIV in the prevention of re-intubation 72 hours after extubation among sepsis patients (Tongyoo et al., 2021). We also use HFNC in the post-extubation period in critically ill pediatric patients in our unit and our rate of post-extubation HFNC use in patients included in our study was 5.6%.

There is not yet a fully accepted or published protocol for HFNC. There are centers that protocolize HFNC management and published studies in this direction. Peterson et al. (Peterson et al., 2021) reported that the HFNC management protocol carried out with respiratory therapists in their study was safe, shortened the duration of HFNC, and shortened the duration of intensive care unit stay. Wiser et al. evaluated patient outcomes before and after the HFNC protocol in their clinic. In their study, the results of 584 patients, 29% of whom were patients with bronchiolitis, they reported that flow reduction was faster, hospitalization time was shorter and failure rate was lower after HFNC protocol (Wiser, Smith, Khallouq, Chen, 2021). In our clinic, the patients were followed up by pediatricians and one pediatric intensive care specialist and the entire team applied standard initial flow rate and FiO_2 in HFNC treatment. The pediatric intensive care specialist made the decision of escalation with weaning or failure in the following process.

Since HFNC is an aerosol-forming procedure, there were reservations at the beginning of the COVID-19 pandemic that the use of HFNC would increase the risk of transmission. However, it was later reported that HFNC was superior to conventional oxygen therapies in terms of oxygenation in COVID-19 patients (Gürün et al., 2020).

With the realization of its benefit to patients, it was recommended that HFNC treatment should be administered in a negative pressure room if possible, if this is not possible, the patient should be isolated in a room and the healthcare personnel should use full personal protective equipment. Numerous studies have reported that HFNC reduces the need for intubation in COVID-19 patients, reduces the length of stay in the intensive care unit and reduces complications related to mechanical ventilation (Gürün et al., 2020; Mellado-Artigas et al., 2021; Ospina-Tascón et al., 2021). In addition, HFNC has been widely used for preoxygenation of patients diagnosed with COVID-19 before intubation during the pandemic period (Gürün et al., 2020).

Our PICU was established in the 3rd month of the pandemic and 16.7% of the patients in our study were patients who underwent HFNC due to COVID19 pneumonia.

Failure of HFNC may lead to delayed intubation and worse clinical outcomes in patients with respiratory failure (Ma et al., 2022). In the literature, recent studies have demonstrated that the HFNC failure rate ranges between 6-24.4% (Frat et al., 2015; Kang et al., 2015; Lee & Nagler, 2017; Ma et al., 2022). In fact, in a study on the use of HFNC in pediatric patients with acute respiratory failure, the failure rate was reported as 37.3%. In the study, it was emphasized that the most important step to be taken in HFNC failure is to switch to invasive mechanical ventilation without delay (Liu et al., 2019). In a retrospective observational study involving 175 adult patients, the overall intensive care mortality and other outcomes of patients with HFNC failure were evaluated. In the study, 2 groups intubated in the first 48 hours and after 48 hours of HFNC administration were compared. Better clinical outcomes and lower mortality rates were reported in the early intubated group (Kang et al., 2015). According to the results of a study reporting HFNC failure rate as 37.3%, PRISM score and $PaCO_2/PaO_2$ were reported to be significantly higher in the HFNC failure group (Liu et al., 2019). In a study on HFNC failure in COVID19 patients, 54 patients were evaluated in an adult study and male gender, low PaO_2/FiO_2 and high SOFA score were independently associated with failure of HFNC treatment in COVID-19 patients (Ma et al., 2022).

There are many studies in the literature on the factors affecting HFNC failure. ROX index is an index used to predict the clinical outcome of HFNC in adult patients defined by Roca et al. ROX index calculated by the formula (SpO_2/FiO_2)/number of breaths >4.88 indicates a low risk of invasive mechanical ventilation (Roca et al., 2016). In the prospective study by Yildizdas et al., it was reported that pediatric ROX index and ROX index variation parameters combined can be used as good markers to predict the risk of HFNC failure in pediatric patients with acute respiratory failure in children undergoing HFNC (Yildizdas, Yontem, Iplik , Horoz & Ekinci, 2021). In a study conducted to predict HFNC failure in the pediatric emergency department, low SpO_2 and SpO_2/FiO_2, on admission, respiratory acidosis and SpO_2/FiO_2 below 195 at 1 hour were shown to be associated with HFNC failure (Er et al, 2018). In a prospective study conducted in PICU, 204 patients who underwent HFNC were evaluated. In this study, HFNC failure rate was reported as 12.7%. A lower SpO_2/FiO_2 ratio on admission has been reported as a predictor of HFNC failure. In addition, study results showed that achievement of a target SpO_2/FiO_2 >200 at 60 minutes significantly predicted HFNC success (Kamit Can et al., 2018). In our study, 12.7% of our patients were intubated as a result of HFNC failure and SpO_2/FiO_2 ratio was significantly lower in intubated patients.

Complications associated with HFNC such as epistaxis, abdominal distension and air leak syndromes have been reported. Selection of an appropriately sized nasal cannula is very important to prevent air leakage (Baudin et al., 2016). In our study, air leakage developed in two patients but resorbed spontaneously without additional intervention when the HFNC was terminated.

The limitations of our study include its retrospective nature, reflecting the experience of a single center and the low number of patients due to incomplete data in the system. The fact that we directly switched to invasive ventilation in HFNC failure was due to the inability to perform noninvasive mechanical ventilation due to resource limitations in our unit. And this situation can be considered as another limitation. The lack of a protocolized HFNC treatment approach in our unit can also be considered among the limitations.

CONCLUSION

HFNC is widely used in PICUs for different indications and etiologies of acute respiratory failure other than bronchiolitis. We think that it would be beneficial to use HFNC in pediatric patients by selecting the appropriate size nasal cannula, paying attention to maximum flow rates, establishing the centers' own HFNC protocols and not delaying the transition to invasive treatment in case of failure.

Note

Our study was presented as an abstract at the 5th one-day pediatricians training meeting of the Turkish National Pediatric Association.

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