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Evaluation of Efficacy and Failure of High Flow Nasal Cannula Therapy in Paediatric Emergency Service and Paediatric Intensive Care Unit

Gizem İleri[1], Neslihan Zengin[2]*, Alkan Bal[3]

1 Dept of Paediatrics, Celal Bayar University Faculty of Medicine, Manisa, TR
2 Div. of Paediatric Intensive Care, Dept of Paediatrics, Celal Bayar University Faculty of Medicine, Manisa, TR
3 Div. of Paediatric Emergency Care, Dept of Paediatrics, Celal Bayar University Faculty of Medicine, Manisa, TR

*** Corresponding Author:** Neslihan Zengin **E-mail:** drneslihanzengin@gmail.com

ABSTRACT

Objective: High-flow nasal cannula oxygen therapy (HFNC) improves gas exchange and decreases work of breathing in patients with acute respiratory distress. We aimed to discuss the indications for HFNC in children of all ages and diagnoses and to evaluate the efficacy and risk factors for failure of HFNC therapy in children with acute respiratory distress and failure in a paediatric emergency service and paediatric intensive care unit (PICU).

Material and Methods: A total of 191 patients aged one month to 18 years treated with HFNC between October 1, 2018, and July 1, 2020, in the Paediatric Emergency Service and PICU were included in the study. Demographic and clinical characteristics, underlying chronic diseases, HFNC treatment success, and treatment failure of the cases were recorded.

Results: One hundred ninety-one children were included in the study, of whom 70 (36.6%) were female, and the median age was 13 months (1-204). The most common indication of HFNC treatment was bronchopneumonia (n=83, 43,5 %). HFNC treatment succeeded in 81.7 % (n=156) of the patients. It was observed that the two most successful patient groups were acute bronchiolitis and pneumonia. The failure rate was 18.3 % (35 of 191 children). The most common underlying comorbidity was bronchopulmonary dysplasia (BPD) (19, 9.9%). There was a statistically significant difference seen on Glasgow Coma Scale (GCS) and lactate value in blood gas in the first hour of the treatment in the group with unsuccessful results ($p<0.05$). During the HFNC treatment, 28 patients (14.7%) required invasive mechanical ventilation (IMV), and seven patients (3.7%) required non-invasive mechanical ventilation (NIMV).

Conclusion: HFNC is a reliable non-invasive treatment modality that is easily tolerated by children and has effective use in many critical diseases. Our study found that HFNC therapy could be initiated as the first-line therapy for various aetiologies of acute respiratory distress in a paediatric emergency service and PICU and all age groups. It was emphasized that transition to other treatment modalities should not be delayed in the cases predicted to be unsuccessful.

Keywords: High-flow nasal cannula, child, acute respiratory distress, paediatric intensive care unit

INTRODUCTION

The reason for over 9 million paediatric emergency service admission is related to respiratory tract diseases. It accounts for approximately 36% of paediatric emergency service admissions. More than 1.5 million children a year are hospitalized due to this issue (1, 2). Pulmonary and extrapulmonary pathologies (congestive heart failure, myocarditis, central nervous system infection, status epilepticus, metabolic diseases, sepsis) may cause respiratory distress. Oxygenation is used in many conditions with a high fraction of inspired oxygen (FiO_2) requirements like carbon monoxide poisoning, pre-intubation, post-extubation, sepsis, acute laryngotracheobronchitis, acute asthma attack, pneumonia, and acute bronchiolitis. The primary parameters are tachypnea, tachycardia, hypoxemia, and respiratory distress. Improvement in vital signs and decline in respiratory distress is not always observed with conventional oxygen treatment (3).

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HFNC treatment allows heated and humidified oxygen to be applied by determining oxygen concentration through a wide nasal cannula with high flow. Oxygen concentration can be increased to nearly 100%, and humidified oxygen temperature can be regulated between 34-37°C, allowing mucociliary clearance to be increased and secretions to be removed easily (3). HFNC has been shown to improve airway resistance and lung compliance, eliminate nasopharyngeal dead space and decrease work of breathing. Effective use of HFNC therapy in infants with respiratory distress, there are many studies showing that it reduces intubation rates and length of stay in PICU. However, few studies highlight the indications for HFNC use, efficacy, and failure factors in older children (4).

Our study aimed to predict HFNC treatment failure in the early period at different diagnosis groups causing respiratory distress and to determine the factors that may indicate not being late for other treatment modalities.

MATERIAL and METHODS

Our study was designed as a single-center retrospective cohort study. Our study included 191 patients aged one month to 18 years who underwent HFNC treatment in the paediatric emergency service and paediatric intensive care unit between October 1, 2018, and July 1, 2020. Acute respiratory distress was defined as hypoxemia (SpO_2<94%) and signs of respiratory distress (increased respiratory rate and heart rate, agitation, change of consciousness, colour changes, nose flaring, retractions, and wheezing) despite standard-flow oxygen therapy.

All patients received standard-flow oxygen therapy before the transition to HFNC therapy. The same brand of nasal cannula and sets were used in paediatric emergency service and PICU, with a flow rate of 1-60 L/min, FiO_2 21-100%, airflow temperature in the range of 34-37°C. FiO_2 was adjusted to reach pulse oximetry (SpO_2) between 92 and 97%, and the flow setting was based on the patients' body weight.

The data registration form noted demographic characteristics of patients, HFNC treatment indication, underlying chronic diseases, treatment success, length of stay in hospital (LOS), and mortality. We also monitored clinical and laboratory parameters, including GCS, respiratory rate per minute (RR/min), heart rate per minute (HR/min), modified respiratory distress assessment instrument score (m-RDAI), SpO_2, SpO_2/FiO_2 (S/F) ratio, venous blood gas for pH and pCO_2 at the beginning and the first hour of the HFNC treatment.

HFNC failure was defined as the need for escalation to NIMV or IMV. The treating physician decided whether escalation of treatment was necessary, but it generally occurred if FiO_2>0.6 or a worsening clinical condition. The patients whose HFNC treatment was discontinued and discharged from the hospital were considered successful.

Statistical Analysis: Statistical analysis was conducted with Statistical Programme Social Sciences (SPSS) 26 package program. Frequency and percent values were used for categorical data.

If the continuous variables complied with normal distribution, mean and standard deviation values were given; on the other hand, if they were not in conformity with normal distribution, their median, minimum and maximum values were stated.

While the continuous variables were analysed in the two groups, the evaluation was carried out with T-test independent groups if they complied with normal distribution; however, it was evaluated with the "Student T" test in independent groups. In assessing consecutive data that were not compatible with normal distribution, the Wilcoxon test was used for independent groups, and the Mann Whitney U test was utilized in independent groups. The significance level was approved as p<0.05 in terms of statistics in our study.

RESULTS

Seventy (36.6%) of the 191 children were female, and the median age was 13 months (1-204). One hundred and two (53.4%) of the 191 children had underlying medical conditions. The most common underlying comorbidity was bronchopulmonary dysplasia (BPD) (19, 9.9%), followed by neurologic disorder, cerebral palsy (CP) (17, 8.9%), and wheezy child (16, 8.4%).

The most common indication for the use of HFNC therapy was pneumonia (83, 43.5%), followed by acute bronchiolitis (49, 25.8%). There were no significant differences in gender, indication, and PRISM III score between the two groups. The success of HFNC treatment in the group ⩽24 months was 88.6%; while it was detected at 69.1% in the group >25 months, the difference between both age groups was statistically significant. The demographics of the 191 children are summarized in **Table I**.

There were significant improvements in RR/min, HR/min, SpO_2, S/F ratio, pH, pCO_2, and lactate values in the first hour of the successful HFNC period (p<0.05) (**Table II**). A statistically significant difference was only seen in GCS when RR/min, HR/min, m-RDAI score, GCS, SpO_2, S/F rate of 35 patients with unsuccessful HFNC were evaluated at the beginning and 1 hour of the treatment (p<0.05). There was a statistically significant difference in the lactate value of 35 patients with HFNC failure who were examined in the baseline and 1st-hour blood gas parameters (p<0.05) (**Table III**).

The two patient groups in which HFNC treatment was most successful were pneumonia (41.7%) and acute bronchiolitis (30.8%) (**Table I**). During the HFNC treatment, 35 patients needed escalation of respiratory support, including 7 (3.7%) who received NIMV and 28 (14.7%) who received intubation with mechanical ventilation. The reasons for treatment failure were a rise in work of breathing, desaturation, weakening of protective airway reflexes, and hemodynamic instability.

While there was no statistically significant difference between successful and unsuccessful groups in terms of duration of HFNC use, there was a significant difference in the length of stay (LOS) in the hospital. No patient was lost during the HFNC treatment process.

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Table I. Demographic characteristics, HFNC indications, success and failure conditions

Patient characteristics	Total n=191(%)	Successfull group n=156(%)	Failure group n=35(%)	P value
Sex				0.947
Female	70 (36.6%)	57 (36.5%)	13 (37.1%)	
Male	121 (63.4%)	99 (63.5%)	22 (62.9%)	
Age				
≤24 months	123 (64.4%)	109 (88.6%)	14 (11.4%)	**0.001**
>25 months	68 (35.6%)	47 (69.1%)	21 (30.9%)	
HFNC indications				0.641
Bronchiolitis Bronchopneumonia	49 (25.8%)	48 (30.8%)	1 (2.9%)	
Lobar pneumonia	83 (43.5%)	65 (41.7%)	18 (51.4%)	
Asthma	16 (8.4%)	12 (7.7%)	4 (11.4%)	
Croup	6 (3.1%)	6 (3.9%)	0 (0%)	
Sepsis	2 (1%)	2 (1.3%)	0 (0%)	
Status epilepticus	14 (7.3%)	8 (5.1%)	6 (17.1%)	
Post-extubation	6 (3.1%)	2 (1.3%)	4 (11.4%)	
Other Indications	6 (3.1%)	5 (3.1%)	1 (2.9%)	
	9 (4.7%)	8 (5.1%)	1 (2.89%)	
PRISM III score	8.70±4.40	8.56±4.32	10.25±4.60	0.112
Escalation of therapy				
NIMV	7 (3.7%)		7 (3.7%)	
IMV	28 (14.7%)		28 (147%)	
Duration of HFNC (day) median (min-max)	2(1-39)	3(1-21)	2(1-39)	0.377
Hospital LOS (day) median (min-max)	5(1-390)	4(1-34)	26(2-390)	**<0.001**

LOS: Length of stay, IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation, HFNC: High flow nasal cannula

Table II. The findings of patients with successful HFNC treatment

Variables	Baseline HFNC treatment Mean (± SD)	First hour HFNC treatment Mean (± SD)	P value
HR/min	147.47 (24.6)	134.14 (18.37)	**0.001**
RR/min	53.67 (15.67)	45.81 (12.85)	**<0.001**
SpO_2	93.4 (5.86)	97.65 (2.29)	**0.001**
S/F rate	194.81 (39.93)	207.86 (32.5)	**<0.001**
pH	7.38 (0.12)	7.41 (0.09)	**0.001**
pCO_2 (mmHg)	36.41 (14.15)	33.62 (9.79)	**0.001**
HCO_3	21.58 (4.12)	22.42 (4.13)	**0.001**
Lactate (mmol/L)	2.25 (1.27)	1,36 (1.09)	**0.001**
	Median (Range)	**Median (Range)**	
GCS	15 (8-15)	15 (12-15)	**0.001**
m-RDAI	6 (3-10)	5 (1-8)	**0.001**

HFNC, high-flow nasal cannula; HR/min heart rate per minute; RR/min, respiratory rate per minute; SpO_2, pulse oximetry; S/F ratio, SpO_2/FiO_2 ratio; GCS: Glasgow coma scale, m-RDAI; modified respiratory distress assessment instrument score (m-RDAI),

Table III. The findings of patients with HFNC treatment failure

Variables	Baseline HFNC treatment Mean (± SD)	First hour HFNC treatment Mean (± SD)	P value
HR/min	145.46 (17.09)	143.14 (18.97)	0.370
RR/min	47.49 (15.72)	47.94 (16.70)	0.776
SpO2	93.14 (4.82)	93.83 (4.64)	0.295
S/F rate	188.42 (37.98)	184.62 (37.41)	0.485
pH	7.37 (0.14)	7.34 (0.16)	0.152
pCO2(mmHg)	38.43 (19.01)	43.45 (22.44)	0.080
HCO3	22.89 (6.68)	23.19 (6.39)	0.150
Lactate (mmol/L)	2.10 (1.86)	1.84 (2.23)	**0.043**
	Median (Range)	**Median (Range)**	
GCS	14 (7-15)	12 (4-15)	**0.048**
m-RDAI	5 (3-9)	6 (3-9)	0.845

HFNC, high-flow nasal cannula; HR/min heart rate per minute; RR/min, respiratory rate per minute; SpO_2, pulse oximetry; S/F ratio, SpO_2/FiO_2 ratio; GCS: Glasgow coma scale, m-RDAI; modified respiratory distress assessment instrument score.

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DISCUSSION

Acute respiratory failure is one of the most important causes of mortality and morbidity. Therefore, early diagnosis and effective treatment are essential. Upper airway pathologies include epiglottitis, laryngotracheitis, subglottic stenosis, foreign body aspiration; lung pathologies like asthma, bronchiolitis, pneumonia, cystic fibrosis; neuromuscular diseases; traumas lead to respiratory failure (5). Oxygen treatment is the most substantial part of treating respiratory distress and respiratory failure. HFNC is a safe, non-invasive, and well-tolerated treatment modality by children used in patients when conventional oxygen treatment is inadequate (3). The number of patients ⩽24 months was 121 (64.4%) in this study. Since the effectiveness and safety of HFNC were proven with studies, it was initiated to be used in many patient groups, especially with bronchiolitis (6-7-8). We found that a higher success rate of HFNC treatment in the ⩽ 24 months is related to the higher incidence of acute bronchiolitis in this age group. Nevertheless, studies related to HFNC use in asthma, pneumonia, croup, neurological diseases, muscle diseases, and cardiac reasons before intubation and post-extubation (9). In a study on HFNC treatment, post-extubation and conventional oxygen treatments were compared by Akyıldız et al., extubation failure rates were found as 4% with HFNC treatment and 22% with conventional oxygen treatment, and HFNC treatment was shown to reduce post-extubation failure risk (10). In studies by Hoffman et al., pneumonia was the most common indication of HFNC treatment (11). The most common indication for the use of HFNC therapy was pneumonia (83, 43.5 %), followed by acute bronchiolitis (49, 25.8%) in our study. In a study; of the patients who had been applied to HFNC treatment in PICU, there was an underlying chronic disease in 55,7 % of patients, and the most commonly seen chronic disease was neuromotor disease at 28.2 % (6). In our study, one hundred and two (53.4%) of the 191 children had underlying medical conditions. The most common underlying comorbidity was bronchopulmonary dysplasia (BPD) (19, 9.9%), followed by neurologic disorder, cerebral palsy (CP) (17, 8.9%). HFNC treatment success rate shows a difference in many studies. Its reason can be indications in its use, age groups, differences in application, and underlying chronic diseases. Success rates of HFNC in literature were varying between 60-94% (12,13,14,8,15,16). In this study, the success rate of HFNC is 82%, and it is similar to the literature. When we look at the treatment results of HFNC treatment indications, acute bronchiolitis forms the most widely used and successful indication in the literature (17). Pneumonia (n=77, 49.4%) and acute bronchiolitis (n=48, 30.8%) were the two most successful indications in the present study. Numerous studies are associated with a length of stay in HFNC treatment. The duration of treatment varies according to underlying comorbid conditions. In a study performed on patients with bronchiolitis by Goh et al., it has been indicated that HFNC treatment reduces hospital stay; however, it does not decrease the LOS in PICU (18). In a study carried out by Mckiernan et al., the average hospital stay in the intensive care unit decreased from 6 days to 4 after HFNC treatment in infants with bronchiolitis (19). In a study carried out by Alessandro et al., it has been seen that long-term HFNC treatment was more successful in patients (15). While there was no significant difference between successful and unsuccessful groups in terms of HFNC treatment duration, it was reported that the hospital length of stay was longer in the unsuccessful group. While HFNC treatment duration was three days in those with no underlying comorbidities, the median hospital LOS was five days. When the median HFNC treatment duration was five days in those with underlying chronic disease, the median hospital stay was seven days. The group with chronic disease had longer hospital stays because they had underlying conditions, and those illnesses were related to specific treatment requirements.

A decrease in RR/min, HR/min, and an increase in SpO2 and S/F ratio in the first hour predict that the treatment will be successful (19). We also observed a decrease in RR/min and HR/min in the first hour. It is essential to follow the SpO2 and S/F ratios in demonstrating the efficacy of treatment in patients treated with HFNC. Studies have shown that S/F ratios are a safe indicator of early NIMV failure in children (20). In a prospective study that a total of 204 cases with HFNC treatment were involved owing to acute respiratory failure by Can et al., the S/F rate elevated in the first hour remarkably, and it was displayed that being over 200 mmHg of S/F rate was a significant criterion in predicting HFNC treatment success (21). We observed a significant increase in SpO2 and S/F ratios in the first hour of treatment in the HFNC successful group. In a study performed by Er et al., after there was no response to HFNC treatment in paediatric emergency service, it was found that if the S/F rate was below 195 in the first hour, it was an early predictor of HFNC treatment failure (22).

In our study, the S/F ratio was below 190 in the first hour of the treatment in the HFNC failure group. When the baseline and first hour data of the HFNC failure group was assessed, a statistically significant difference was only observed in GCS and lactate. We think that the deterioration in GCS in patients with poor airway protective reflexes associated with underlying neurological diseases was significant in estimating failure as other parameters. M-RDAI is a clinical scoring system including wheeze, retraction, RR/min, and skin colour used in many studies regarding bronchiolitis. A study that analyzes the alteration of the m-RDAI score with HFNC treatment stated that treatment failure was higher in inpatient groups with an mRDAI score of >5 and emphasized the importance of m-RDAI score in the prediction of treatment achievement (15). While the m-RDAI score median value was six before the treatment, it was 5 in the first hour of the treatment, and it displayed a significant reduction in HFNC successful group. If possible, blood gas monitoring is an important follow-up parameter to evaluate the efficiency of ventilation and oxygenation in respiratory failure. In a study that Söğütlü et al. assessed the efficacy of HFNC treatment, there was no significant difference in pH and pCO_2 before and after the treatment (3). In a study that Vural et al. evaluated 131 patients who had been applied HFNC treatment in PICU, while there was no significant difference in pH and pCO_2 in blood gases of cases, a significant difference was established in their blood lactate levels (6). In the present study, while a statistically significant difference was observed in pH, pCO_2, HCO_3, and lactate values in the patient group with successful results, a significant difference was observed statistically in only the blood lactate levels of the patient

group with failure. Blood lactate value is a fast, simple, measurable parameter in determining tissue hypoxia, and it has prognostic importance. The significant difference in lactate values in the baseline and first hour blood gas parameters in the HFNC failure group; has been associated with conditions such as shock, seizures, and hypoxemia, leading to decreased oxygen delivery to tissues.

There are many studies related to intubation and mortality during HFNC treatment. While HFNC treatment use was related to reducing intubation and IMV rate in PICU, no alteration occurred in mortality in studies performed (23-24).

In a study, it has been indicated that there was an intubation need in 12% of the patients who had been applied HFNC (25). However, in the present study, 28 (14.7%) patients were intubated; other NIMV methods were used in 7 (3.7%) patients.

HFNC treatment has been used increasingly in respiratory failure in paediatric patients. However, more comprehensive, randomized, and controlled studies are required to determine its reliability and effectiveness more precisely and ascertain the factors affecting the utilization failure of HFNC, ensure the early transition to other treatment modalities and reduce hospital stay and cost.

Limitations: The main limitations of our study are that it was designed retrospectively, and data quality was dependent on file contents. As it was a retrospective study, patients' long-term flow and FiO2 values could not be accessed, and the onset and endpoint of HFNC treatment and FiO2 values could not be indicated in the study. Our study did not include the patients whose data were inadequate or could not be accessed.

CONCLUSION

We think that HFNC can be initiated as the first-line therapy for all age groups of children with various aetiologies of acute respiratory distress in paediatric emergency service and PICU. Further prospective studies are needed to evaluate the risk factors for failure in different clinical conditions and the reliability of long-term use.

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Ethical approval: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Local Ethical Committee. All procedures performed in studies with human participants met the ethical standards of the Institutional Research Commission and the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards.

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