

Indications and Safety of High Flow Nasal Cannula in Pediatric Intensive Care Unit: Retrospective Single Center Experience in Saudi Arabia

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Background: High flow nasal cannula (HFNC) is a new device for respiratory support. Its use continues to increase in pediatrics as its system is easily set up and well tolerated by patients. We aimed in this study to explore indications and safety of HFNC use and predictors of HFNC failure.

Methods: Hospital records of 92 children with acute respiratory distress admitted to the pediatric intensive care unit (PICU) in Abha Maternity and Children Hospital from January 2018 until March 2020 and received HFNC therapy were studied. A data collection sheet was used that included patients' age, gender, the indication of HFNC, associated chronic diseases, previous admission to PICU, vital signs (initially, 8 hours and 48 hours after using HFNC), outcome after using HFNC, and reasons for HFNC failure.

Results: After receiving HFNC, children's respiratory rate, heart rate, systolic blood pressure, and oxygen saturation improved significantly ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.005$, and $p < 0.001$, respectively). Regarding laboratory findings, pH and serum bicarbonate improved significantly ($p < 0.001$ for both), while PaCO₂ improved but not significantly. The failure rate of HFNC was 23.0%. HFNC failure rates were significantly higher among children with chronic diseases than those with no chronic disease (33.3% and 14.9%, respectively, $p = 0.038$) and among children with the air-leak syndrome ($p < 0.001$). After 48 hours of HFNC use, children who experienced HFNC failure had significantly higher respiratory and heart rates ($p < 0.001$ and $p = 0.018$, respectively), lower diastolic blood pressure ($p = 0.011$), and higher PaCO₂ ($p < 0.001$).

Conclusion: After HFNC use, significant improvements occur in all clinical parameters and laboratory values of children with respiratory distress, but about one-fourth of cases may experience HFNC failure. Predictors for HFNC failure include underlying chronic disease, low diastolic blood pressure, high respiratory rate, high heart rate, high initial PaCO₂.

Keywords: high flow nasal cannula, respiratory distress, pediatric intensive care, Saudi Arabia

Introduction

Acute lower respiratory illnesses constitute the leading cause of death among children aged less than five years. Despite the beneficial effects of mechanical ventilation in reducing mortality rates, these technologies are rarely available in many countries due to their high cost and the need for trained personnel for their use. However, the high flow nasal cannula (HFNC), a noninvasive respiratory support tool, proved to be of growing applicability in children with an acute lower respiratory infection (ALRI), hypoxemia, and respiratory distress.¹⁻⁴

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HFNC is quite safe and an effective treatment option for acute respiratory distress. The HFNC mechanism of action involves decreasing nasopharyngeal resistance, washout of dead space, a reduced inflow of ambient air, and increased airway pressure.⁵ It can reduce the need for intubation and mechanical ventilation in children with severe lower respiratory illness.^{1,2,4} During the last few years, there has been a wide range of HFNC use, especially for patients with severe asthma exacerbation, pneumonia, bronchiolitis, congenital heart disease, and post-extubation respiratory distress.^{6,7} Within 1–2 hours, good responders to HFNC show improvement in their respiratory rate, heart rate, and work of breathing, and reductions in apnea and O₂ requirements.^{8,9} However, if no improvement was observed within this period, another respiratory support and transfer to intensive care unit are deemed.^{1,2,9}

Independent risk factors and predictors for HFNC failure include high FiO₂ requirements, previous intubation, cardiac comorbidity,¹⁰ lack of early oxygenation improvement,^{1,2} low initial pH, and a high initial PaCO₂.¹¹ In Montreal, Canada, Baudin et al reported an HFNC failure rate of 22% among children who were admitted to the PICU of the university-affiliated Sainte-Justine Hospital and were treated with high flow nasal cannula, 3% received tracheal intubation, while 19% required to transition to noninvasive ventilation.¹² However, using HFNC following clinical protocols in PICUs was associated with low complication rates, eg, pneumothorax requiring chest tube insertion (1%), chest tube-related air leaks (3%), and significant epistaxis (0.6%).¹²

Studies on HFNC in Saudi Arabia are scarce. In Riyadh, Saudi Arabia, Tareq et al reported their experience using HFNC at the Pediatric Intensive Care Unit (PICU) of King Faisal Specialist Hospital and Research Center (KFSH-RC). Pneumonia was the main reason for HFNC use (45.5%). In their cohort, the failure rate of HFNC was 24.6%. They concluded that HFNC is beneficial for children admitted to pediatric ICU. It reduces the rate of intubation and improves the survival rate. It is a well-tolerated device and should be considered as initial respiratory support delivered at pediatric PICU.¹³ In our PICU, we have been using HFNC as the initial respiratory support for children with acute respiratory distress for a couple of years. The present study aimed to explore indications and safety of HFNC use and predictors of HFNC failure.

Methods

Study Population

The study included 92 children hospitalized between January 2018 and March 2020 and received HFNC therapy due to acute respiratory distress. Enrolled children aged between 1 month and 12 years old. Patients who presented with shock or intubated without receiving HFNC were excluded. Failure of HFNC was considered if the patient's respiratory condition did not improve or even worsened and the patient needed escalation to noninvasive ventilation or intubation and mechanical ventilation in the intensive care unit.¹⁰ The decision for discontinuation of HFNC and initiation of mechanical ventilation was based on the clinical and laboratory assessment of the patients by a certified pediatrician.

As per the international guidelines of HFNC use in children, the rate of 30L/min was considered the maximum flow.¹⁴ Detailed children hospital course was registered, which included death, or successful separation from HFNC, defined as discontinuation of HFNC after more than 48 hours or until PICU discharge.¹⁵

Study Design and Setting

The present study followed a retrospective research design. Children were hospitalized at Abha Maternity and Children Hospital (AMCH), Southwest of Saudi Arabia. AMCH is considered tertiary care, referral, and teaching hospital in the southwestern region of the Kingdom of Saudi Arabia. It is a 15-bed medical and surgical pediatric intensive care unit and receives patients from 20 peripheral hospitals.

Data Collection

We used a data collection sheet that included patients' age, gender, the indication of HFNC, associated chronic diseases, previous admission to PICU, and vital signs (initially, 8 hours, and 48 hours after using HFNC). In addition, the outcomes after using HFNC (clinical improvement or escalation to invasive ventilation) and complications of HFNC (pneumothorax, epistaxis, and severe abdominal distension).

Statistical Analysis

The Statistical Package for Social Sciences (IBM-SPSS, version 25) was used for data entry and statistical analysis. The Shapiro–Wilk test was used to study variables' normality. Quantitative variables were presented as mean \pm SD, while categorical variables were presented as

frequency and percentage. For comparing results of the HFNC failure group with those of the HFNC success group, a chi-square test was applied to compare categorical variables, while an independent sample *t*-test was used to compare quantitative variables. Moreover, repeated measures analysis of variance test was applied to assess the significance of the change in quantitative variables (clinical and laboratory findings) after 8 and 48 hours. Significant differences were considered at *p*-values less than 0.05.

Ethical Approval

The study was approved by the Institutional Research Ethics (IRE) board, Abha Maternity and Children Hospital ethical committee, Saudi Arabia. It was carried out according to the Declaration of Helsinki. Patients' informed consents were not needed since this study was a retrospective observational study without any interventions.

Results

Demographics of the Enrolled Subjects

Table 1 shows that 48.9% of participant children were less than 12 months old, and 56.5% were males. Associated chronic diseases were present among 48.9% of children, including underlying congenital heart diseases, bronchial asthma, and chronic respiratory insufficiency due to cerebral palsy and neuromuscular disorders. The most common indications for HFNC were bronchopneumonia alone (40.2%) or associated with bronchiolitis (13%), while 12% had severe asthma exacerbation, and 23.9% were post-extubation. More than half of participant children (56.5%) received FiO₂ less than 50%, while 39.1% of children received FiO₂ 50–60%. The duration of hospital stays of 19.6% was 1–7 days, that of 39.1% was 8–14 days, while that of 15.2% was 15–21 days, and that of 26.1% was more than 21 days. Regarding the duration of stay at PICU, 57.6% stayed for 1–7 days, 17.4% was 8–14 days, while 8.7% was 15–21 days, and 16.3% was more than 21 days. About one-fourth of children (27.2%) were previously admitted to PICU. About one-fifth of children (23%) failed HFNC and underwent tracheal intubation. The readmission to the PICU occurred in 15.2% of those who needed HFNC.

The Initial Clinical Characteristics and Laboratory Parameters of the Patients

Table 2 shows that after receiving HFNC, respiratory rate, heart rate, systolic blood pressure, and oxygen saturation

Table 1 Demographics and Clinical Characteristics of the Enrolled Patients

Characteristics	n (%)
Age groups	
< 12 months	45(48.9)
1–5 years	35(38.0)
5 years	12(13.0)
Gender, male, No. (%)	52(56.5)
Associated chronic diseases	45(48.9)
Indication for HFNC use	
Bronchopneumonia	37(40.2)
Bronchopneumonia + bronchiolitis	12(13.0)
Post-extubation	22(23.9)
Severe asthma exacerbation	11(12.0)
Others	10(10.9)
Fraction of inspired oxygen (FiO ₂)	
<50%	52(56.5)
50–60%	36(39.1)
>60%	4(4.3)
Duration of hospital stay	
1–7 days	18 (19.6)
8–14 days	36 (39.1)
15–21 days	14 (15.2)
>21 days	24 (26.1)
Duration of stay at PICU	
1–7 days	53 (57.6)
8–14 days	16 (17.4)
15–21 days	8 (8.7)
>21 days	15 (16.3)
Previous admission to PICU	25 (27.2)
Complications	
Air leak syndrome	8 (8.7)
Death	9 (9.8)
Interventions	
Tracheal intubation	21 (23.0)
Chest tube insertion	8 (8.7)
Outcome	
Success	71 (77.0)
Failure	21 (23.0)

Abbreviations: HFNC, High Flow Nasal Cannula; FiO₂, Fraction of inspired oxygen; PICU, Pediatric Intensive Care Unit.

of children at PICU improved significantly ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.005$ and $p < 0.001$, respectively), after 8 hours of receiving HFNC. Regarding laboratory findings, pH and serum bicarbonate improved significantly ($p < 0.001$ for both) after 8 hours of receiving HFNC, while PaCO₂ improved but not significantly ($p=0.069$).

Table 2 Clinical and Laboratory Findings of Enrolled Children at Different Timing of HFNC Initiation (Pre-HFNC and POST-HFNC at 8 and 48 Hours)

Variables, Mean \pm SD	Initially	After 8 Hours	After 48 Hours	P value
RR (per minute)	51.2 \pm 11.8	41.5 \pm 9.5	40.0 \pm 10.8	<0.001*
HR (per minute)	139.7 \pm 25.8	123.2 \pm 19.2	121.9 \pm 22.7	<0.001*
SBP (mmHg)	103.5 \pm 16.8	97.0 \pm 14.1	96.9 \pm 14.4	<0.001*
DBP (mmHg)	59.2 \pm 13.1	56.1 \pm 14.3	53.5 \pm 11.5	0.005*
Oxygen saturation	90.7 \pm 11.1	97.3 \pm 3.9	97.0 \pm 4.1	<0.001*
pH	7.35 \pm 0.08	7.39 \pm 0.07	7.41 \pm 0.06	<0.001*
PaCO ₂ (mmHg)	39.3 \pm 9.7	37.4 \pm 10.3	37.0 \pm 7.9	0.069
Serum bicarbonate (μ mol/L)	21.4 \pm 3.9	22.5 \pm 3.8	23.4 \pm 3.7	<0.001*

Note: *P < 0.05 (significant).

Abbreviations: HFNC, High Flow Nasal Cannula; SD, Standard Deviation; RR, Respiratory Rate; HR, Heart Rate; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; PaCO₂, Partial pressure of carbon dioxide.

Characteristics of Patients with Failed and Succeeded HFNC Intervention

Table 3 shows that failure rates for HFNC did not differ significantly according to child's age, gender, indication for HFNC use, received FiO₂, or previous admission to PICU. The failure rate for HFNC was significantly higher among children with chronic diseases than those with no chronic disease (33.3% and 14.9%, respectively, p=0.038). Failure rates for HFNC were significantly higher among children with a hospital stay or stayed at PICU for more than two weeks (p < 0.001 for both).

Comparisons Between the Initial 8 Hours and 48 Hours Clinical and Laboratory Parameters of Patients with Failed and Succeeded HFNC Intervention

Table 4 shows that the respiratory rate (Mean \pm SD) of children after 48 hours of HFNC administration was significantly higher among those with HFNC failure than those with HFNC success (47.5 \pm 14.9 and 37.6 \pm 7.9%, respectively, p < 0.001). Heart rate (Mean \pm SD) of children after 48 hours of HFNC administration was significantly higher among those with HFNC failure than those with HFNC success (131.9 \pm 22.5 and 118.8 \pm 22.0, respectively, p=0.018). Diastolic blood pressure (Mean \pm SD) of children after 48 hours of HFNC administration was significantly lower among those with HFNC failure than those with HFNC success (48.1 \pm 10.7 and 55.1 \pm 11.3, respectively, p=0.011). Levels of partial pressure of carbon dioxide (Mean \pm SD) of children after 8 and 48 hours of HFNC administration were significantly higher among those with HFNC failure than those with

HFNC success (44.2 \pm 11.5 and 42.4 \pm 9.8 vs 35.3 \pm 9.0 and 35.4 \pm 6.5, respectively, p < 0.001 for both). Serum levels of bicarbonate (Mean \pm SD) of children after 8 and 48 hours of HFNC administration were significantly higher among those with HFNC failure than those with HFNC success (23.9 \pm 4.8 and 25.4 \pm 5.2 vs 22.0 \pm 3.3, and 22.8 \pm 2.9, p=0.042, and p=0.003, respectively).

Adverse Effects of HFNC in Our Study

In our cohort, there were nine deaths, all of which had severe cardiopulmonary comorbidities. Furthermore, they required prolonged PICU admission and intubation for several days following the failure of the HFNC. Due to severe air leak syndrome, eight patients required chest tube insertions. The pneumothorax occurred in one of the HFNC patients, while the other patients were intubated.

Discussion

The present study revealed that the main indications for HFNC utilization at PICU were respiratory distress due to bronchopneumonia, bronchiolitis, severe asthma exacerbation, or post-extubation. It has been noted that within 8 hours after HFNC use, there were significant improvements in all clinical and laboratory findings of children who received HFNC. However, few complications were reported, eg, air leak syndrome (8.7%) and death (9.8%).

Invasive ventilation becomes indicated when respiratory support with HFNC seems inadequate. However, invasive ventilation frequently has a high risk for subsequent complications, such as ventilator-associated pneumonia, airway stenosis, sepsis, acute respiratory distress syndrome, atelectasis, or pulmonary edema.^{16–18} However, HFNC has recently

Table 3 Clinical Characteristics of Patients by HFNC Status (Non-Failure vs Failure)

Variables	Non-Failure (n=71)		Failure (n=21)		P value
	No.	%	No.	%	
Age groups					0.812
<12 months	34	75.6	11	24.4	
1–5 years	26	74.3	9	25.7	
>5 years	10	83.3	2	16.7	
Gender					0.780
Male	39	75.0	13	25.0	
Female	31	77.5	9	22.5	
Associated chronic diseases					0.038*
No	40	85.1	7	14.9	
Yes	30	66.7	15	33.3	
Indication for HFNC use					0.283
Bronchopneumonia	28	75.7	9	24.3	
Bronchopneumonia+ bronchiolitis	9	100.0	0	0.0	
Severe asthma exacerbation	5	62.5	3	37.5	
Post-extubation	8	66.7	4	33.3	
Status asthmaticus	3	100.0	0	0.0	
Others	6	60.0	4	40.0	
FiO ₂					0.420
<50%	41	78.8	11	21.2	
50–60%	27	75.0	9	25.0	
>60%	2	50.0	2	50.0	
Duration of hospital stay					<0.001*
1–7 days	16	88.9	2	11.1	
8–14 days	36	100.0	0	0.0	
15–21 days	10	71.4	4	28.6	
>21 days	8	33.3	16	66.7	
Duration of stay at PICU					<0.001*
1–7 days	49	92.5	4	7.5	
8–14 days	15	93.8	1	6.3	
15–21 days	4	50.0	4	50.0	
>21 days	2	13.3	13	86.7	
Previous admission to PICU					0.591
No	50	74.6	17	25.4	
Yes	20	80.0	5	20.0	
Air leak syndrome					<0.001*
No	69	82.1	15	17.9	
Yes	1	12.5	7	87.5	

Note: *P < 0.05 (significant).

Abbreviations: HFNC, High Flow Nasal Cannula; FiO₂, Fraction of inspired oxygen; PICU, Pediatric Intensive Care Unit.

gained rapid global adoption and became well documented in intensive and emergency health-care settings.^{19,20}

Several studies have indicated that HFNC is a simple, well-tolerated noninvasive respiratory support.^{1,2,20} It improves gas exchange and flushes anatomical dead space, and decreases work of breathing.²¹ Therefore, HFNC is considered the primary respiratory support for patients with hypoxemic acute respiratory failure across ages.²¹ Coletti et al stated that HFNC could be started as the first-line management for several diseases among children, such as bronchial asthma, or pneumonia, with a low failure rate of 10.1%, necessitating either noninvasive ventilation (5.6%) or required intubation (4.5%).⁶ However, a recent study reported that the effectiveness of HFNC as initial respiratory support among children with moderate-to-severe acute viral bronchiolitis was less than that of nasal continuous positive airway pressure (nCPAP).²² They suggested that nCPAP may be more efficient than HFNC for initial respiratory support in young infants hospitalized in a PICU for moderate-to-severe acute viral bronchiolitis. Nevertheless, respiratory support with either nCPAP or HFNC is relatively safe, with very low intubation rates, air leak syndrome, or death.²²

Moreover, HFNC can be used for patients in several clinical environments, such as emergency departments, inter-hospital transport, or intensive care units. It is reasonably simple to set up, with a single interface, only two settings (gas-flow and FiO₂), and no synchronization.²³

The failure rate for HFNC utilization in our study was 23.9%. Several studies have reported that the overall failure rate for HFNC therapy in the PICU and pediatric emergency department are 30% and 39%, respectively.^{24,25}

Our study indicated that failure rates for HFNC in children admitted to PICU were characterized by the presence of associated chronic disease and those with the hospital stay more than two weeks. In addition, lower diastolic blood pressure, higher respiratory and heart rates at 48 hours, and elevated initial PaCO₂.

Several studies described children with failed HFNC as younger, those with tachypnea, high PaCO₂, a low initial venous pH less than 7.30,^{11,26} experienced no improvement in heart rate,²⁷ or respiratory rate,²⁶ and those with respiratory acidosis.^{9,11,26} On the other hand, Schibler et al reported that predictors of HFNC success were a significant and rapid decrease in heart rate from baseline within 60 min of HFNC initiation and similarly significant improvement in respiratory rate.¹⁹

Table 4 Vital Signs and Laboratory Characteristics of Patients by HFNC Status (Non-Failure vs Failure)

Variables, Mean \pm SD	Non-Failure (n=71)		Failure (n=21)		P value
	Mean	SD	Mean	SD	
RR/min (initial)	50.5	11.9	53.3	11.4	0.328
RR/min (after 48 hours)	37.6	7.9	47.5	14.9	<0.001*
HR/min (initial)	138.7	24.2	143.0	30.7	0.498
HR/min (after 48 hours)	118.8	22.0	131.9	22.5	0.018*
DBP (mm/Hg, after 48 hours)	55.1	11.3	48.1	10.7	0.011*
PaCO ₂ (mm/Hg, initial)	38.7	10.0	41.4	8.9	0.250
PaCO ₂ (mm/Hg, after 8 hours)	35.3	9.0	44.2	11.5	<0.001*
PaCO ₂ (mm/Hg, after 48 hours)	35.4	6.5	42.4	9.8	<0.001*
HCO ₃ (mmol/L, initial)	21.0	3.7	22.5	4.1	0.109
HCO ₃ (mmol/L, after 8 hours)	22.0	3.3	23.9	4.8	0.042*
HCO ₃ (mmol/L, after 48 hours)	22.8	2.9	25.4	5.2	0.003*

Note: *P < 0.05 (significant).

Abbreviations: HFNC, High Flow Nasal Cannula; SD, Standard Deviation; RR, Respiratory Rate; HR, Heart Rate; DBP, Diastolic Blood Pressure; PaCO₂, Partial pressure of carbon dioxide; HCO₃, Serum bicarbonate.

In our study, the most common indications for HFNC were bronchopneumonia associated with bronchiolitis, severe asthma exacerbation, and children with respiratory distress post-extubation. Several studies reported similar indications, including asthma,²⁵ bronchiolitis,^{4,7,22,26–28} pneumonia,¹¹ congenital heart diseases,²⁹ and post-extubation with respiratory distress.³⁰ HFNC utilization is associated with decreased intubation rates, reduced respiratory distress, and increased oxygenation saturation.^{19,31,32}

Compared with CPAP, HFNC use in the PICU and neonatal ICU is associated with better tolerance, reduced nasal/mucosal injury, ease of use, fewer complications, and lower cost.^{30,33,34} Baudin and Pouyau stressed that HFNC is generally used and preferred more than nCPAP by many clinicians, who strongly prefer to use HFNC due to its perceived benefits over nCPAP, eg, greater comfort, higher simplicity, and more effectiveness.²⁰ Therefore, HFNC found its place in the hearts of many physicians, including pediatric intensivists and respiratory therapists.

The study has several limitations. First, the study is a retrospective study and was conducted in a single center, which increased the chance of bias and limited the study generalization. Also, we did not include a scoring system to classify the severity of patient's illnesses at the beginning of the HFNC initiation.

Conclusion

The main indications for HFNC utilization for children admitted to the PICU in Abha Maternity and Children Hospital are bronchopneumonia, bronchiolitis, status asthmaticus, or post-extubation. After HFNC use, significant

improvements occur in all clinical and laboratory results. However, few complications may occur, eg, air leak syndrome, or death. About one-fourth of cases may experience HFNC failure. Predictors associated with HFNC failure include the presence of chronic disease, hospital stays more than two weeks, having air leak syndrome, low diastolic blood pressure, high respiratory rate, high heart rate, and high PaCO₂.

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Disclosure

The authors declare no conflicts of interest for this work.

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