RESEARCH PAPER

High Flow Nasal Cannula Therapy as a Primary Mode of Respiratory Support in a Pediatric Intensive Care Unit

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Objective: To assess efficacy and safety of High flow nasal cannula therapy (HFNC) as primary mode of treatment for children with respiratory distress. **Methods:** Consecutive patients (1 mo-16 years) with respiratory distress were assessed for respiratory clinical score, COMFORT score and saturation to FiO_2 (SF) ratio. **Results:** A total of 188 (91.7%) patients out of 205 responded to HFNC alone. The respiratory clinical score and COMFORT score were lower with higher SF ratio in these than 17 patients who required ventilation (P<0.001). Median (IQR) time to failure was 2 (1.75-24) hours. Air leak was seen in 2 (1%) patients. **Conclusions:** HFNC is an effective and safe primary mode of respiratory support in children with respiratory distress. Children who succeed on HFNC show a favorable clinical response within first few hours.

Keywords: *Comfort score, Mechanical ventilation, Non-invasive ventilation, SaO2/FiO2 ratio*.

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Humidified flow nasal cannula (HFNC) delivers heated and humidified gas mixture at a flow greater than patient's inspiratory flow demand and can provide intermediate level of support between low-flow oxygen delivery and non-invasive ventilation (NIV) in critically ill children [1]. Retrospective studies have shown that HFNC is useful for conditions like bronchiolitis, asthma, pneumonia and congenital heart disease [2]. The evidence for its safety or usefulness in children is limited [3]. There is paucity of prospective clinical trials on the effectiveness of HFNC in respiratory failure (not due to bronchiolitis) in pediatric intensive care unit (PICU).

This study aimed at assessing the efficacy and safety of HFNC as a primary mode of treatment in respiratory distress in children.

METHODS

This cross-sectional study was undertaken at an urban tertiary care hospital of Western India from 1 January, 2018, to 31 December, 2018. The study was approved by the institutional ethics committee and informed consent from parents was taken prior to enrollment. Consecutive patients with respiratory distress necessitating admi-ssion to PICU, in the age group of 1 month to 16 years of age were included. Children requiring immediate non-invasive (NIV) or invasive ventilation and those with contraindications to HFNC, altered sensorium (GCS <12), apnea and catecholamine resistant shock were excluded.

Respiratory distress was defined as hypoxia (SpO2 <94% in room air), tachypnea (as per age) and increased work of breathing (chest wall retractions, use of accesssory muscles of breathing and nasal flaring/grunting). HFNC was started as the first line treatment if all the above clinical signs were present. Primary outcome measure was need for 'NIV' or invasive ventilation.

Bronchiolitis was defined as a clinical syndrome of respiratory distress in children less than two years with rhinorrhea followed by lower respiratory infection resulting in wheezing and crepts. Children with fever, respiratory distress, tachypnea and infiltrates on chest radiograph were classified as pneumonia. Children with fever, respiratory distress, tachypnea and chest signs of wheezing and crepts but without infiltrates on chest radiograph were classified as LRTI with wheeze.

A respiratory clinical score with the following parameters was calculated: age specific respiratory rate scores 0 to 3, retractions 0 to 3, dyspnea 0 to 3, and wheeze 0 to 3. Total score ranged between 0 for normal and 12 at the extremes [4]. FiO2 was adjusted to keep arterial oxygen concentration between 92-97% to calculate saturation to FiO2 (SF) ratio. HFNC tolerance

was assessed using modified COMFORT scale [5]. The scale estimates eight parameters with a 1 (low) to 5 (high) score: alertness, calmness, respiratory response, physical movement, mean arterial pressure, heart rate, muscle tone, and facial tension. The total score can range between 8-40 (score of 17-26 suggesting good comfort). Respiratory clinical score, SF ratio and modified COMFORT score were calculated before starting HFNC treatment, at 60 to 90 minutes and 12-24 hours afterward.

HFNC system (Fisher and Paykel Healthcare, New Zealand) with junior circuit 900PT501 was used. Infant OPT316 or Pediatric OPT318 nasal prongs were selected as per child's age. Flow was initiated at 1-2 L/kg/min for infants and 1 L/kg/min for pediatric patients and adjusted according to patient response and tolerance (max 2 L/kg/min). Failure on HFNC was defined as need for NIV or invasive ventilation, when clinical deterioration was present. Criteria for intubation were respiratory arrest, refractory hypoxia (SpO2 <90% on 100% FiO2), exhaustion due to increased work of breathing and inability to protect airway. Criteria for switching to NIV were left to discretion of the attending intensivist.

For calculation of sample size, a baseline risk for need of ventilation as 16% was assumed in children with respiratory distress presenting to the emergency. We hypothesised that HFNC would reduce the risk by 50% (absolute reduction of 8 percentage points). Using alpha error of 0.05 and for 90% power, we calculated a sample size of 178. To allow for potential 10% recruitment failure rate, required sample size was increased to 200.

Statistical analyses were performed using IBM SPSS 23 version (IBM 2015), and significance was assessed at 0.05 level. Comparisons between two groups were made using independent sample Mann Whitney U test and Kruskall Wallis test for continuous measurements. Univariable and multivariable Cox regression models were used to assess the association of HFNC failure with various clinical parameters.

RESULTS

A total of 205 (71 girls) children were commenced on HFNC therapy. HFNC failure occurred in 17 (8.3%) children at a median (IQR) time of 2 (1.75-24) hours. Thirteen of these children required invasive ventilation. Three children developed local erythema and two developed airleak on HFNC. Clinical characteristics of responders and non-responders to HFNC are presented in **Table I**.

Table I Characteristics of Children as per Response to High Flow Nasal Cannula (HFNC)

	HFNC responders (n=188)	*Non-responders (n=17)*	*P value*
Age, n (%)			
<6 mo	38 (90.4)	4 (9.6)	0.01
6-23 mo	60 (90.9)	6 (9.1)	0.001
2-5 y	73 (94.8)	4 (5.2)	0.001
6-12 y	15 (83.3)	3 (16.7)	0.001
13-16 y	2 (100)	0	0.001
Diagnosis, n (%)			
Bronchiolitis	37 (97.3)	1 (2.6)	0.001
Pneumonia	54 (79)	14 (21)	0.001
LRTI with wheezing	17 (94.5)	1 (5.5)	0.001
Acute severe asthma	15 (100)	0	0.001
Congenital heart disease	7 (100)	0	0.001
Septic shock	41 (93.1)	3 (6.9)	0.001
Others	15 (100)	0	0.001
FiO2 (%)[a]	40 (35-45)	60 (55-70)	0.08
Flow (L/min)[a]	15 (11-20)	16 (13-22)	0.45
PIM2 score (%)[a]	2.7 (1.1-6.4)	5 (4-14.3)	0.01
Mortality	0	3 (17.6)	0.001
Duration of HFNC (h)[a]	48 (41-75)	2 (1.75-24)	0.001
Respiratory clinical score[a]			
On admission	10 (9-11)	12 (11-12)	0.001
At 60-90 min	9 (8-10)	12 (11-12)	0.001
At 12-24 h	7 (6-8)	12 (11-12)	0.001
SF ratio[a]			
On admission	316 (262-330)	260 (236-323)	0.03
At 60-90 min	333 (281-346)	245 (217-246)	≤0.001
At 12-24 h	360 (306-374)	245 (196-252)	≤0.001
COMFORT score[a]			
On admission	31 (29-33)	33 (32-35)	≤0.001
At 60-90 min	29 (27-30)	33 (32-35)	≤0.001
At 12-24 h	25 (24-26)	34 (32-35)	≤0.001

[a]*Data presented as median (IQR); SF: Saturation to FiO2 ratio; LRTI: Lower respiratory tract infection; Maximum HFNC parameters – Oxygen flow rate (FiO2); PIM 2 score: Pediatric index of mortality score.*

In univariate regression analysis, respiratory clinical score [Hazard ratio (95% CI) 4.9 (2.1-11.2), *P*=0.001]; SF ratio [HR (95% CI) 0.94 (0.97-0.99), *P*=0.012]; and COMFORT score, [HR (95% CI)1.99 (1.4-2.8), *P*= 0.001] on admission were associated with HFNC failure. In multivariable regression analysis, none of these parameters were associated with increased risk of HFNC failure, respiratory clinical score [HR (95% CI) 2.26 (0.84-7.7), *P*=0.09], SF ratio, [HR (95% CI) 0.99 (0.97-1.00), *P*=0.29] and COMFORT score [HR (95% CI) 1.39 (0.88-2.21), *P*=0.15].

WHAT THIS STUDY ADDS?

- HFNC is an effective mode of respiratory support in children with respiratory distress with heterogenous etiologies.

DISCUSSION

HFNC was effective in preventing intubation in children with respiratory distress in the present study with low failure rate in patients with various respiratory etiologies. The low failure rate on HFNC could be because was started relatively early and preemptively, even in cases of mild to moderate illness.

Patients with shock were also managed successfully on HFNC in this study. The contribution of HFNC in recovery of these patients cannot be quantified since multimodal monitoring and management plays a more important role. However, HFNC helps in decreasing work of breathing in these patients by maintaining functional residual capacity.

Patients who responded on HFNC had lower respiratory clinical score and COMFORT score with higher SF score at 60-90 minutes and at 12-24 hours. These parameters suggest that patients who are likely to succeed on HFNC would show favorable response within first few hours which was sustained over 24 hours. Non-responders had lower SF ratio, higher respiratory clinical score and COMFORT score on admissions suggesting that these children were sicker and more likely to need NIV or invasive ventilation.

The complication rate was low with airleak seen in only two patients with ARDS. The lower incidence of airleaks may be due to the standard flow rates being used in the study.

HFNC use requires additional treatment modalities before invasive ventilation which can be associated with adverse events [6] and additional costs. It may also be associated with delay in intubation, which however, was not seen in the present study.

The present study used easily reproducible tools for assessment and monitoring of severity of illness in children with heterogenous conditions making this relevant in daily clinical practice. This was however, a single center study using prespecified protocol, thereby limiting its external validity. A control arm without HFNC was not compared for ethical concerns.

To conclude, HFNC is an effective and safe primary mode of respiratory support in children with respiratory distress due to various causes. Children who succeed on HFNC show favourable response within first few hours and response is sustained over the next few days.

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