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Original Research Article

An Analytical Study to Evaluate the Efficacy and Safety of High Flow Nasal Cannula Therapy as a Primary Mode of Respiratory Support in a Pediatric Intensive Care Unit

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Abstract

Aim: To assess efficacy and safety of High flow nasal cannula therapy (HFNC) as primary mode of treatment for children with respiratory distress.

Material & Methods: This cross-sectional study was undertaken at Department of Pediatrics, NMCH, Patna, Bihar, India, over a period of one year. Consecutive patients with respiratory distress necessitating admission to pediatric intensive care units(PICUs), in the age group of 1 month to 16 years of age were included.

Results: A total of 220 (105 boys, 115 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. In univariate regression analysis, respiratory clinical score [Hazard ratio (95% CI) 4.1 (2.2-11.7), P=0.001]; SF ratio [HR (95% CI) 0.98 (0.94-0.98), P=0.01]; and COMFORT score, [HR (95% CI) 1.98 (1.6-2.0), P= 0.001] on admission were associated with HFNC failure.

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.

Introduction

Respiratory support is the most common organ support therapy provided in pediatric intensive care units(PICUs); nearly 75% of the 18,000 children admitted annually to PICUs in the United Kingdom and Ireland receive some form of respiratory support [1]. Over the past decade, concerns regarding the complications of invasive ventilation (IV) have prompted greater use of non-invasive respiratory support (NIRS) modes such as continuous positive airway pressure (CPAP) [2–4]. Although the use of NIRS

has been shown to improve patient outcomes in randomized controlled trials (RCTs) in adult and neonatal intensive care [5–8], there is a dearth of RCTs in the PICU setting [9, 10].

High-flow nasal cannulas (HFNCs) are an increasingly used form of non-invasive respiratory support, and they have shown potential in reducing the need for intubation [11-14]. HFNCs enable the administration of high concentrations of oxygen with adequate relative humidity and temperature, and they have been shown to improve airway resistance and lung compliance, achieve a certain level of continuous positive airway pressure (CPAP), eliminate dead space and decrease respiratory work [15-16]. HFNC therapy has been used in infants with respiratory distress syndrome and infants with bronchiolitis, and it has been shown to decrease respiratory distress and intubation rates, increase patient comfort and ease of use compared with face masks or traditional cannulas, and shorten the length of stay in pediatric intensive care units (ICUs) [17-18].

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

Material & Methods:

This cross-sectional study was undertaken at Department of Pediatrics, NMCH, Patna, Bihar, India, over a period of one year.

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 admission 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 accessory 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, and 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 [19]. 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 [20]. 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 hypothesized 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 25 version (IBM 2017), 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 220 (105 boys, 115 girls) children were commenced on HFNC therapy. HFNC failure occurred in 15 (6.81%) children at a median (IQR) time of 2 (1.75-24) hours. 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)

Variables	HFNC responders (n=205)	Non- responders (n=15)	P value
Age, (n)			
<6 mo	38	3	0.01
6-23 mo	53	5	0.001
2-5 y	89	4	0.001
6-12 y	23	3	0.001
13-16 y	2	0	0.001
Diagnosis, n (%)			
Bronchiolitis	38(97.94%)	1 (2.56%)	0.001
Pneumonia	60 (80%	15(20%)	0.001
LRTI with wheezing	15 (93.75%)	1 (6.25%)	0.001
Acute severe asthma	13 (100%)	0	0.001
Congenital heart disease	10 (100%)	0	0.001
Septic shock	44(95.65%)	2(4.35%)	0.001
Others	21 (100%)	0	0.001
FiO2 (%)[a]	43	64	0.229
Flow (L/min)[a]	18	18	0.582
PIM2 score (%)[a]	2.6	4	0.01
Mortality	0	2	0.001

Duration of HFNC (h) [a]	40	1	0.001
Respiratory clinical score[a]			
On admission	11(10 -12)	13 (12-13)	0.001
At 60-90 min	10 (9- 11)	13 (12-13)	0.001
At 12-24 h	8 (7 -9)	13 (12-13)	0.001
SF ratio[a]			
On admission	310 (268-333)	260 (236-323)	0.03
At 60-90 min	329 (287-354)	245 (217-246)	≤0.001
At 12-24 h	378 (312-380)	245 (196-252)	≤0.001
COMFORT score[a]			
On admission	30 (28-32)	31 (30-33)	≤0.001
At 60-90 min	28 (26-29)	31 (30-33)	≤0.001
At 12-24 h	22 (21-24)	32 (30-33)	≤0.001

(a= Data presented as mean)

In univariate regression analysis, respiratory clinical score [Hazard ratio (95% CI) 4.1 (2.2-11.7), P=0.001]; SF ratio [HR (95% CI) 0.98 (0.94-0.98), P=0.01]; and COMFORT score, [HR (95% CI) 1.98 (1.6-2.0), 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) 2.49 (0.83-7.9), P=0.382], SF ratio, [HR (95% CI) 0.99 (0.97- 1.00), P=0.301] and COMFORT score [HR (95% CI) 1.40 (0.88-2.40), P=0.721]. [Table 1]

Discussion:

HFNC therapy is most commonly used for infants with acute viral bronchiolitis. However, recent studies have suggested that HFNC therapy can also be effectively and safely used in patients with a wider age range and etiologies of respiratory distress [21-25]. Coletti et al. investigated the use of HFNC in 620 children with a wide range of indications in their pediatric ICU, including a significant number of subjects with status asthmaticus (41%) and congenital heart disease with respiratory distress (10%), and they reported that 10.1% of the cases needed escalation of therapy to either non-invasive ventilation or intubation with mechanical ventilation [25].

Kelly et al. also reported the use of HFNC therapy in 496 children with respiratory distress in the emergency department, including 46% with bronchiolitis, 28% with pneumonia and 8% with asthma. They reported that 8% of the cases failed therapy and required intubation with mechanical ventilation following HFNC therapy [23].

In this pilot trial, performed in advance of a large definitive RCT, we clarified three important areas of uncertainty: whether PICU clinicians would be willing to randomize participants considering that HFNC may be superseding CPAP as the first-line choice for NIRS in pediatric settings [26]; whether the study algorithms were acceptable to clinicians and practical to use, considering the variability in current practice relating to the use of HFNC/CPAP [27]; and whether we could identify a suitable patient-centred and clinically relevant primary outcome measure, considering that previous RCTs of HFNC have focused on surrogate outcome measures such as crossover or treatment failure [28-32].

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.

Conclusion:

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.

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