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Outcome of high-flow nasal cannula therapy in children with acute respiratory distress in a tertiary care centre: A prospective cohort study

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***Abstract*---**Background: High-flow nasal cannula (HFNC) therapy is a relatively non-invasive new therapy for respiratory distress and has shown potential in reducing invasive ventilation. Recent studies have suggested that HFNC therapy can also be effectively and safely used in patients having respiratory distress with a wider age range of severity and etiologies. Aim: To assess the outcomes of patients placed on a high flow nasal cannula as a primary mode of treatment for children with respiratory distress. Methods: This is a prospective observational study was conducted on patients with acute respiratory distress who require hospitalization in Age groups from 1 month to 12 years old between August 2021 and December 2021 at Tertiary Pediatric Center in Hyderabad. The study was approved by the ethical committee and parental consent was obtained prior to initiation. We calculated a sample size of 350 using 0.05 alpha error and 90% power. Statistical analysis was performed using IBM SPSS23 version (IBM 2015) and significance was assessed at the 0.05 level. Results: A total of 362 children (176girls and 186boys) started HFNC therapy. The HFNC failure occurred in 20 (5.5%) children after a median (IQR) time of 2 (1.75-24) hours. Twenty of these children needed invasive ventilation.

Five children developed localized erythema and two developed air leaks under HFNC. Conclusions: HFNC is an effective and safe primary mode of respiratory support for children with respiratory distress due to various causes. Children who succeed with HFNC respond positively within the first few hours, and the response lasts for the next few days. Therefore, even community health centers across India are advised to use HFNC whenever indicated in a pediatric critical care center, as many poor people are unable to attend a tertiary care center.

***Keywords*---**Comfort Score, Clinical Respiratory Score (CRS), High flow nasal cannula, Respiratory distress.

Introduction

Acute respiratory distress is the most common cause of admission to the pediatric intensive care unit. Respiratory distress was defined as hypoxia (SpO2 < 94% room air), tachypnea, and increased respiratory work (chest wall contraction, accessory respiratory muscle use, and nasal flaring/groaning) [1]. "The incidence of ARDS in children is 3.5 per 100,000 general population and 2.3 per 100,000 children each year in the PICU [2]. It is a childhood emergency and can be caused by an infection, chronic illness, or airway obstruction. Of these causes, acute bronchiolitis and pneumonia are the leading causes of shortness of breath in children [3]. High-flow nasal cannula (HFNC) therapy is a new, relatively non-invasive treatment for shortness of breath and has shown the potential to reduce invasive ventilation [4]. HHFNC has been suggested to reduce the work of breathing and improve the effects of ventilation through multiple mechanisms, such as Reduced inspiratory work of breathing by providing increased airflow, Reduced metabolic cost of gas conditioning, Washout of nasopharyngeal dead space, and Provision of end-distending pressure in lungs[5]. HFNC is very comfortable for children as it provides a more effective treatment and can open collapsed alveoli and increase the functional residual capacity (FRC) of the lungs. [6]. Recent studies have shown that HFNC therapy was originally used for acute bronchiolitis, but can be used effectively and safely in patients of a wide range of ages and etiologies with dyspnea [7]. Predict the success or failure of HFNC therapy usingthe ROX Index using SaO2, FiO2, and a simple bedside tool that uses respiratory rate. The higher ROX index value was associated with the success of HFNC. Contraindications to HFNC therapy include low pH respiratory acidosis (<7.25), nasal obstruction, eg choanal atresia, trauma, air leaks (such as pneumothorax), and life-threatening hypoxia. This study aims to evaluate the efficacy and safety of HFNC as the primary treatment for respiratory distress in children.

Methods

This is a prospective observational study conducted between August 2021 and December 2021 at the Tertiary paediatricsCenter of Niloufer Hospital in Hyderabad. The study was approved by the Institutional Review Board and parental consent was obtained prior to registration.

The inclusion criteria:

1. Age from 1 month to 12 years old.
2. Patients with acute respiratory distress who require hospitalization in the PICU for any period of hospitalization.

The exclusion criteria:

1. Children less than 1 month and 13 years or older
2. Children who required immediate non-invasive ventilation or invasive ventilation.
3. Altered sensorium.

We also monitored clinical parameters such as heart rate, respiratory rate, SpO2, and venous blood gas at pH and CO2. FiO2 was adjusted to maintain arterial oxygen levels between 94 to 97% to calculate the saturation/FiO2 (SF) ratio. HFNC system (Fisher and Paykel Healthcare, NewZealand) with junior circuit 900PT501 was used, AND Inspired [SMITH] were used. Infant OPT316 or Paediatric OPT318 nasal prongs were selected as per the child's age. The flow starts at 1-2 L / kg / min for infants and 1 L / kg / min for paediatric patients and is tailored to the patient's response and tolerability (up to 2 L / kg / min).

Disease severity and oxygenation were ascertained by using a modified comfort score, respiratory clinical score (RCS), S / F ratio (SpO2 / FiO2), and ROX index score [(SpO2 / FiO2) / RR] [8]. Measured and calculated initially than every 4 hours of the first 48 hours after the start of HFNC therapy or before discontinuation of HFNC therapy.

The modified COMFORT score can assess HFNC tolerance. 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. Overall scores range from 8 to 40 (a score of 17-26 indicates good comfort)[9]. The clinical breathing score (CRS) [10] was calculated using the following parameters: age-specific respiratory rate (0-2), room air spo2 (0-2), use of accessory muscles (0-2): , Auscultation (0 -2), mental state (0-2) and color (0-2). Shortness of breath can be categorized as mild (<3), moderate (4-7), and severe (8-12) based on the total score.

NIV or INVASIVEVENTILATION were the primary endpoint. The failure of HFNC was defined as requiring NIV or mechanical ventilation in the presence of clinical deterioration. The criteria for intubation were respiratory failure, refractory hypoxia (SpO2 <90% on 100% FiO2), fatigue from respiratory work, and inability to protect the airways. The criteria for switching to NIV were left to the discretion of the treating intensivist.

The sample size calculation assumed a baseline risk of requiring 16% ventilation for children with shortness of breath in an emergency. The HFNC assumed a 50 percent reduction in risk (an absolute 8 percent reduction). We calculated a sample size of 350 using 0.05 alpha error and 90% power. The required sample size has been increased to 400 to account for the potential 10% recruitment failure rate. Statistical analysis

was performed using IBM SPSS23 version (IBM 2015) and significance was assessed at the 0.05 level. Comparisons between the two groups were made using the independent Mann-Whitney U and Kruskal-Wallis tests for continuous measurements. The univariate and multivariate Cox regression models were used to evaluate the association between HFNC failures and various clinical parameters.

Table 1. Guide for Initiation and Escalation of HHFNC Therapy

Parameters	1 – 4 years	5 years and above
Initial settings	10L per minute and FiO2 of 40%	12L per minute and FIO2 of 40%
First escalation of therapy*	Increase flow rate to 12L per minute	Increase flow rate to 16L per minute
Second escalation of therapy*	Increase FiO2 to 50% if SpO2 <92%	Increase FiO2 to 50% if SpO2 <92%
Third escalation of therapy*	Increase flow rate to 15L per minute	Increase flow to 20L per minute
Fourth escalation of therapy*	Increase FiO2 as needed to maintain SpO2 >92% with referral to PICU	Increase FiO2 as needed to maintain SpO2 >92% with referral to PICU
Maximum Flow**	15 L/min	20 L/min

Weaning therapy

Consideration of weaning of HHFNC can be made when the patient is no longer felt to be in moderate severe respiratory distress. Weaning can be performed as outlined below:

- First wean Fi02 to 40%.
- Monitor and document Sp02, RR, HR and respiratory distress (if any) after each change in Fi02.
- Inform senior nursing and medical staff if there is any deterioration in respiratory/cardiovascular status — therapy may need to be increased.
- Once the child is stable and in a Fi02 of 40% standard low flow nasal cannula oxygen can be used, there is no need to wean flow rate (Flow rate can be weaned at the discretion of the supervising Consultant if felt to be warranted).

Signs of Stabilization

Within two hours clinical signs of stabilization should be seen and can be measured according to the following parameters:

- Fio_2 required to maintain the Spo_2 in the target range should decrease to <40%.
- Heart rate should reduce by 20% or be within the normal range for age.

- Respiratory rate should reduce by 20% or be within the normal range for age.
- Clinical signs of respiratory distress should improve (e.g recessions, nasal flaring, tracheal tug).
- Consider a repeat CBG/VBG

Acute Deterioration on HHFNC

Urgent medical review required if any of the following occur:

- Sudden worsening of respiratory distress and/or Sp02 - urgent CXR should be performed to exclude a pneumothorax.
- Recurrent/frequent apnoea and or bradycardia.
- Persistent hypoxaemia despite adequate escalation of Fi02/Flow or Sudden deterioration in patient's overall condition.

Results

A total of 362 children includes 48.61% of girls (n=176) and 51.38% boys (n=186) started on HFNC therapy. The HFNC failure occurred in 20 (5.52%) children after a median (IQR) time of 2 (1.75-24) hours. Twenty of these children needed invasive ventilation. Five children developed localized erythema and two developed air leaks under HFNC. Clinical characteristics of responders and non-responders to HFNC are presented in **Tables 2, 3, 4 and 5**.

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

Table 2. Age distribution of HFNC responders and non responders

Age	*HFNCresponders (n=342)*	*Non- responders (n=20)*	*P value*
<6 months	105(94.59%)	6 (5.4%)	0.01
6-23 months	95(94.05%)	6 (5.9%)	0.001
2-5 years	97(96%)	4(3.96%)	0.001
6-12 years	45(91.83%)	4 (8.16%)	0.001

Table 3. Diseases distribution of HFNC responders and non-responders

Diagnosis	HFNC responders (n=342)	Non-responders (n=20)	P value
Bronchiolitis	111(95.6%)	5 (4.3)	0.001
Pneumonia	171(94.4%)	10 (5.5)	0.001
Acute severe asthma	8 (80%)	2(20%)	0.001
Congenital heart	20 (100%)	0	0.001

disease			
dengue	23(95.83%)	1(4.16%)	0.001
post ventilated	9(81.81%)	2(18.18%)	0.001

Table 4. Settings of HFNC

	HFNC responders	*Non- responders*	*P value*
FiO2 (%)	40 (35-45)	70 (55-70)	0.08
Flow (L/min)[a]	15 (11-20)	16(13-22)	0.45
Mortality	0	5 (17.6)	0.001
Duration of HFNC (h)[a]	48 (41-75)	2 (1.75-24)	0.001

[a]Data presented as median (IQR); SF: Saturation to FiO2 ratio; LRTI: Lower respiratory tract infection; Maximum HFNC parameters

Table 5. Scores

Respiratory clinical score[a]			
On admission	8 (8-11)	12 (11-12)	0.001
At 6 hrs	8 (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 6 hrs	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	30 (29-33)	33 (32-35)	≤0.001
At 60-90 min	25 (25-30)	33 (32-35)	≤0.001
At 12-24 h	24 (24-26)	34 (32-35)	≤0.001

[a]SF: Saturation to FiO2 ratio;[a]Data presented as median (IQR);

Discussion

HFNC was effective in preventing intubation in pediatric patients with respiratory distress in this study and had a low failure rate in patients with various respiratory etiologies. The low failure rate of HFNC may be due to the preemptive initiation of the HFNC, even mild to moderate illness, relatively early. A total of 362 (boys (186) are more affected) patients were commenced on HFNC. The most common indication for the use of HFNC therapy is pneumonia (94.4%), followed by bronchiolitis (95.6%), which responded to HFNC in more than 90% of cases, similar to the study conducted by Chang CC [11]. In this study, children under 2 years were more responsive to HFNC (n = 200). HFNC failure occurred in 20 patients who were later commenced on NIV OR Invasive ventilation. HFNC helps to reduce the respiratory work of these patients by maintaining residual functional capacity. Patients who responded to HFNC had lower respiratory clinical scores at admission, 6 hr and 24 hrs(median 8), lower

COMFORT scores (median beign 30,25,24 at admission, 6 and 24 hrs) and higher SF scores at 6 and 12-24 hours (median benign 333 and 360) . 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 (n=20) had a low SF ratio, a high respiratory clinical score, and a high COMFORT score on admission. Fio_2 in responders was 40-50 (Median 45) and in non responders 65-75(70) This suggests that these children are ill and are likely to require NIV or invasive ventilation. The incidence of complications was low, and air leaks were observed in only two patients with ARDS. The mortality rate for this study was 1.38% (n=5). The reduced occurrence of air leaks may be due to the standard flow rates used in the study. Kepreotes reported HFNC is less likely to cause treatment failure in children with respiratory disabilities when compared to traditional oxygenation using a low fluid nasal cannula (100% oxygen at 2 L / min flow)[12]. Meta-analysis and systematic review by Lin Who compared HFNC with standard oxygen therapy, and showed that HFNC had fewer treatment failures than standard oxygen therapy[13].

HFNC use requires additional treatment modalities before invasive ventilation which can be associated with adverse events 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.

Conclusion

HFNC is an effective and safe primary mode of respiratory support for children with dyspnea due to various causes. Children who succeed with HFNC respond positively within the first few hours, and the response lasts for the next few days. Therefore, even community health centers across India are advised to use HFNC whenever indicated in a pediatric critical care center, as many poor people are unable to attend a tertiary care center.

References

1. Shah S, Kaul A, Bhosale R, Shiwarkar G. High flow nasal cannula therapy as a primary mode of respiratory support in a pediatric intensive care unit. Indian Pediatrics. 2021 Jan;58(1):41-3.
2. Kadafi KT, Yuliarto S, Monica C, Susanto WP. Clinical review of High Flow Nasal Cannula and Continuous Positive Airway Pressure in pediatric acute respiratory distress. Annals of Medicine and Surgery. 2021 Dec 14:103180
3. Ghazaly MM, Abu Faddan NH, Raafat DM, Mohammed NA, Nadel S. Acute viral bronchiolitis as a cause of pediatric acute respiratory distress syndrome. European journal of pediatrics. 2021 Apr;180(4):1229-34.
4. Zhao H, Wang H, Sun F, Lyu S, An Y. High-flow nasal cannula oxygen therapy is superior to conventional oxygen therapy but not to noninvasive mechanical ventilation on intubation rate: a systematic review and meta-analysis. Critical care. 2017 Dec;21(1):1-2.

5. Document Reference: HHFNC-11-2015-AWDC-V1, Humidified High Flow Nasal Cannula (HHFNC) oxygen therapy: A guide for ward and ED based use in patients with acute viral bronchiolitis Last Updated: November 2015
6. Kwon JW. High-flow nasal cannula oxygen therapy in children: a clinical review. Clinical and Experimental Pediatrics. 2020 Jan;63(1):3.
7. Spentzas T, Minarik M, Patters AB, Vinson B, Stidham G. Children with respiratory distress treated with high-flow nasal cannula. Journal of intensive care medicine. 2009 Sep;24(5):323-8.
8. Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard JD, Masclans JR. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: The utility of the ROX index. Journal of critical care. 2016 Oct 1;35:200-5.
9. Maaskant J, Raymakers-Janssen P, Veldhoen E, Ista E, Lucas C, Vermeulen H. The clinimetric properties of the COMFORT scale: a systematic review. European Journal of Pain. 2016 Nov;20(10):1587-611.
10. Nayani K, Naeem R, Munir O, Naseer N, Feroze A, Brown N, Mian AI. The clinical respiratory score predicts paediatric critical care disposition in children with respiratory distress presenting to the emergency department. BMC pediatrics. 2018 Dec;18(1):1-8.
11. Chang CC, Lin YC, Chen TC, Lin JJ, Hsia SH, Chan OW, Lee EP. High-Flow Nasal Cannula Therapy in Children with Acute Respiratory Distress with Hypoxia in A Pediatric Intensive Care Unit-A Single Center Experience. Frontiers in Pediatrics. 2021;9:375
12. Kepreotes, E., Whitehead, B., Attia, J., Oldmeadow, C., Collison, A., Searles, A., Goddard, B., Hilton, J., Lee, M. and Mattes, J., 2017. High-flow warm humidified oxygen versus standard low-flow nasal cannula oxygen for moderate bronchiolitis (HFWHO RCT): an open, phase 4, randomised controlled trial. *The Lancet*, *389*(10072), pp.930-939].
13. Lin J, Zhang Y, Xiong L, Liu S, Gong C, Dai J. High-flow nasal cannula therapy for children with bronchiolitis: a systematic review and meta-analysis. Archives of disease in childhood. 2019 Jun 1;104(6):564-76