Research Article

High-Flow Nasal Cannula versus Conventional Oxygen Therapy in Children with Respiratory Distress

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Abstract

Purpose: The aim of this study is to determine the clinical efficacy of high-flow nasal cannula (HFNC) therapy compared with conventional oxygen therapy in children presented with respiratory distress. **Study Design:** This was a randomized controlled study. **Materials and Methods:** Infants and children aged between 1 month to 5 years who were admitted to our tertiary referral center for respiratory distress (July 1, 2014 to March 31, 2015) and met the inclusion criteria were recruited. **Interventions:** Infants and children hospitalized with respiratory distress were randomized into two groups of interventions. All clinical data, for example, respiratory score, pulse rate, and respiratory rate were recorded. The results were subsequently analyzed. **Results:** A total of 98 respiratory distress children were enrolled during the study period. Only 4 children (8.2%) failed in HFNC therapy, compared with 10 children (20.4%) in conventional oxygen therapy group ($P = 0.09$). After adjusted for body weight, underlying diseases, and respiratory distress score, there was an 85% reduction in the odds of treatment failure in HFNC therapy group (adjusted odds ratio 0.15, 95% confidence interval 0.03–0.66, $P = 0.01$). Most children in HFNC therapy group had significant improvement in clinical respiratory score, heart rate, and respiratory rate at 240, 360, and 120 min compared with conventional oxygen therapy ($P = 0.03$, 0.04, and 0.03). **Conclusion:** HFNC therapy revealed a potential clinical advantage in management children hospitalized with respiratory distress compared with conventional respiratory therapy. The early use of HFNC in children with moderate-to-severe respiratory distress may prevent endotracheal tube intubation. **Trial Register:** TCTR 20170222007.

Keyword: Children, conventional oxygen, high flow nasal cannula, intubation, respiratory distress

Introduction

Respiratory distress is one of the most common causes of hospitalization in children worldwide.[1] Various forms of oxygen therapy are used to treat children who have respiratory distress. Oxygen supplement by nasal cannula in infants and children is limited by flow due to insufficient humidification. If oxygen flow was used more than 2-6 L/min, it will make cool and dry the airway.[2,3] Noninvasive positive pressure ventilation was proved to reduce the need for endotracheal tube intubation, but it could make patient discomfort. Mechanical ventilation through an endotracheal tube is another choice for acute respiratory failure, but it could be associated with various complications, including nosocomial pneumonia and prolonged pediatric Intensive Care Unit (PICU) stay. Currently, high-flow nasal cannula (HFNC) therapy has been increasingly used in a variety of clinical settings.[4-6]

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Quick Response Code:

Website: www.ijccm.org

DOI: 10.4103/ijccm.IJCCM_181_17

It can deliver heated and humidified oxygen to the nose at a high-flow rate and adjust the fraction of inspired oxygen (FiO_2) by changing the fraction of oxygen in the driving gas. It could reduce work of breathing by providing adequate flow, supplying adequately warmed and humidified gas, washing out of nasopharyngeal dead space, and providing distending pressure.[7-9] It was recently studied in a preterm neonate with respiratory distress syndrome and revealed that it was able to reduce the intubation rate.[10] In addition, there was evidence that using HFNC in acute bronchiolitis could reduce intubation rate.[11]

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How to cite this article: Sitthikarnkha P, Samransamruajkit R, Prapphal N, Deerojanawong J, Sritippayawan S. High flow nasal cannula versus conventional oxygen therapy in children with respiratory distress. Indian J Crit Care Med 2018;22:321-5.

Frat *et al*. revealed a significant difference in favor of high flow oxygen therapy in 90 days mortality compared to standard oxygen therapy in treating adult nonhypercapnic respiratory failure.[12] A randomized controlled trial (RCT) done by Testa *et al*. reported a benefit of using HFNC in pediatric cardiac surgical patients.[13] However, there is still lacking of clinical evidence in the management of critically ill children. Thus, the aim of this study was to determine the clinical efficacy of HFNC therapy compared with conventional oxygen therapy in children presented with respiratory distress.

Materials and Methods

Study design

This study was a prospective RCT in children aged 1 month to 5 years admitted to a tertiary care referral center with respiratory distress between July 1, 2014 and March 31, 2015. The study protocol was approved by the Institutional Review Board, (No. 187-57). Informed consents were obtained from the study participants before being formally enrolled into the study.

Population

Infants and children who were admitted to our hospital due to respiratory distress (respiratory rate [RR] greater than normal, signs of increased work of breathing or oxygen saturation in room air below than 95%) were enrolled into the study.[14] The exclusion criteria's were a clinical respiratory failure that required immediate invasive or noninvasive mechanical ventilation, hemodynamic instability, congenital cyanotic heart diseases, the presence of air leak syndrome, nasal mucosa injury, or refused to participate.

Randomization

Infants and children were randomly assigned to each study group through opaque sealed envelopes in fixed-block method process by computer. They were random to two strategies, HFNC therapy, and conventional oxygen therapy. Then, they were managed with either treatment at general pediatric ward or PICU.

Study procedure

In HFNC therapy group, it was delivered by high-flow oxygen together with blender and heat humidification system (MR850 heated humidifier, Fischer and Paykel Healthcare) and adjusted FiO_2 from 0.21 to 1 to achieve of at least 95% oxygen saturation. Nasal cannulas were applied to the prong outer diameter occupy about 50% of the nares internal diameter. The initial flow rate for HFNC was determined by the current infant weight (as Royal Children's Hospital Melbourne guideline).[15] The flow rate was started at 6 L/min and increased until continuous air flow was heard at basal lungs bilaterally. The maximum flow rate was calculated by body weight (kg) if the body weight was lower than 10 kg, the maximum flow rate was set at 2 L/kg/min. If the body weight was higher than 10 kg, the maximum flow rate was set at 2 L/kg/min for the first 10 kg and plus 0.5 L/kg/min for each kg thereafter (maximum flow 30 L/min). FiO_2 was started at 0.6 and titrated up to keep oxygen saturation greater than 95%. The settings of HFNC therapy were adjusted by assigned doctors (fellows of pediatric pulmonary and critical care).

Transition to conventional oxygen therapy was recommended when clinical condition had improved as indicated by decreasing work of breathing and having normal or improving RR. First, the FiO_2 was weaned to 0.3 to keep oxygen saturation greater than 95%. Then, we further reduced flow by half, if the patients were tolerated then we changed to low flow oxygen therapy.[13]

In conventional oxygen therapy group, oxygen therapy was applied continuously through nasal cannula limited flow rate at 2 L/min, face mask or oxygen box depend on clinical severity. The rate is adjusted to maintain oxygen saturation greater than 95%.

Criteria's for the failure of the treatment

If the children could not achieve any two or more of these criteria's: RR reduction by 20% or to within normal range, heart rate (HR) reduction by 20% or to within normal range, and FiO_2 <0.5, they were defined as failure of treatment and considered noninvasive positive pressure ventilation or intubation.[14]

Data collection

Data collected included sex, age, body weight, underlying diseases, diagnosis, and complications of therapies administered were collected. Data of RR, pulse rate, oxygen saturation, and respiratory distress score at presentation, after intervention at 30, 60, 90, and 120 min then every 1 h for 4 h, every 4 h for 12 h, and every 8 h until 48 h were recorded.[15]

Statistical analysis

All data are presented as a mean and standard deviation. Study groups were compared using the Chi-square or Fisher's exact test for categorical variables. Independent *t*-test was used for continuous variables with normal distribution and Mann–Whitney U-test where distribution was skewed. Logistic regression was used to estimate differences between the groups in risk, after controlling for confounding factors. Results from the logistic models are expressed as adjusted odds ratios with exact 95% confidence intervals (CIs). To determine whether there was an impact of time since initiation of treatment on the change in the physiological variables, multilevel mixed-effects linear regression was used. All data were analyzed with Stata (version 12; StataCorp, College Station, Texas, USA).

Results

A tota of 177 children were admitted to our hospital due to respiratory distress between July 1, 2014 and March 31, 2015, 79 children were excluded from the study [Figure 1]. Ninety-eight children participated in the study, 49 children were assigned to HFNC therapy and 49 children to conventional oxygen therapy. Baseline demographic characteristics and

clinical parameters before study entry were comparable in both groups [Table 1]. Children in HFNC therapy group had body weight lower than conventional oxygen therapy group. Most of the children in HFNC group had more underlying diseases compared to the control group, Respiratory diseases were the most common underlying diseases in children enrolled in this study. The major cause of acute respiratory distress was pneumonia, which was diagnosed in 72 children (73%) and was similar in both groups. However, the initial respiratory score was significantly higher in HFNC group than in conventional oxygen therapy group.

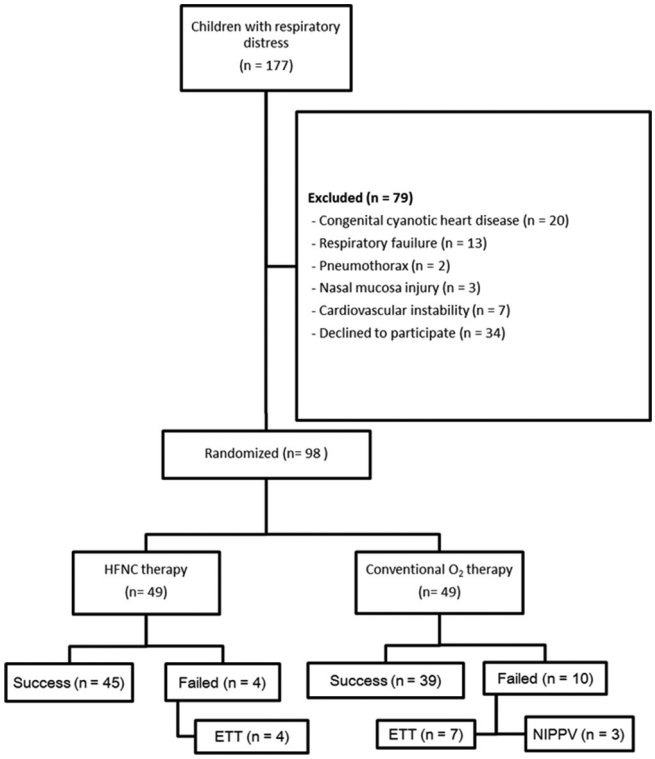

Figure 1: Flow diagram demonstrate how children enrollment into study

Only four children (8.2%) failed in HFNC therapy compared to 10 children (20.4%) in conventional oxygen therapy group ($P = 0.09$). After adjusted for body weight, underlying diseases, and respiratory distress score, there was an 85% reduction in the odds of treatment failure in HFNC therapy group (adjusted odds ratio 0.15, 95% CI 0.03-0.66, $P = 0.01$) compared to control.

Children in HFNC therapy group had significant improvement in RR after 120 min of intervention ($P = 0.03$) [Figure 2]. Clinical respiratory distress score in HFNC therapy group was significantly decreased compared to conventional oxygen therapy group after 240 min of intervention ($P = 0.03$) [Figures 3 and 4].

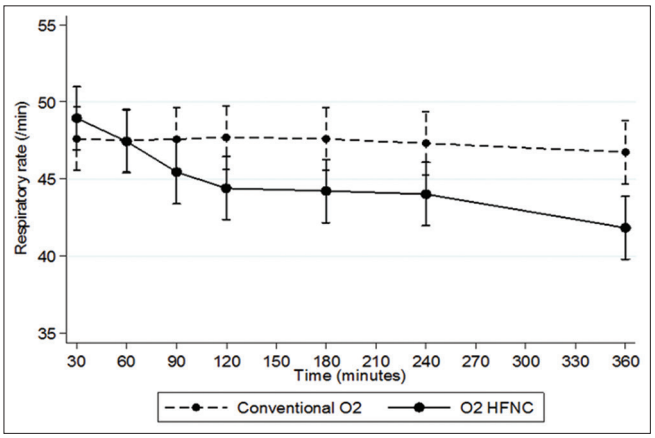

Figure 2: Graph shows respiratory rate after the treatment compare between high flow nasal cannula and conventional group

Table 1: Demographic data

Data	HFNC therapy ($n=49$)	Conventional O_2 therapy ($n=49$)	*P*
Age (months)	16.7±12.6	20.7±14.0	0.11
Male (*n*)	27 (55)	23 (47)	0.42
Body weight (kg)	8.3±3.1	9.9±2.7	0.01*
Diagnosis, *n* (%)			
Pneumonia	36 (73.5)	36 (73.5)	0.607
Bronchiolitis	12 (24.5)	10 (20.4)	
Other	1 (2)	3 (6.1)	
Underlying disease, *n* (%)			
No underlying disease	14 (28.6)	26 (53.0)	0.036*
Respiratory disease	12 (24.5)	14 (28.6)	
Neuromuscular disease	10 (20.4)	5 (10.2)	
Hepatobiliary disease	8 (16.3)	2 (4.1)	
Other	5 (10.2)	2 (4.1)	
Respiratory score	9.0±1.1	8.1±1.1	<0.001*
O_2 saturation (%)	92.4±3.3	93.4±3.1	0.12
Respiratory rate (tpm)	49.0±8.4	46.5±7.2	0.11
Heart rate (bpm)	146.6±19.8	141.9±20.5	0.25
Body temperature (°C)	37.52±0.8	37.83±1.0	0.09

*$P<0.05$, statistically significant. HFNC: High-flow nasal cannula

We also looked at different factors that might assist to predict early failure. We found that children who failed HFNC therapy had a higher respiratory score at 60 min after treatment compared to the successful group ($P = 0.02$) [Figure 5].

There was no serious adverse event observed during the study in both groups. Only one child in HFNC therapy group had epistaxis after using HFNC for 36 h.

Discussion

The study revealed a potential clinical advantage of using HFNC in management children hospitalized with respiratory distress compared with conventional respiratory therapy. Most children recruited for this study were diagnosed with pneumonia. The failure rate in HFNC therapy group was 8.2% compared to 14.3% in conventional oxygen therapy. McKiernan *et al*. recently reported a retrospective study, they found that children diagnosed with acute bronchiolitis had a significant reduction in intubation rate from 23% to 9% following the introduction of HFNC.[11] In addition, another retrospective study by Schibler *et al*. observed the increasing use of HFNC therapy in children with acute bronchiolitis caused a significant reduction in intubation rate from 37% to 7%.[14]

Testa *et al*. revealed a potential benefit of using HFNC in children postcardiac surgery. In this study, using HFNC therapy can prevent intubation (odds ratio 0.15; 95% CI 0.03–0.66; $P = 0.01$) compared to conventional oxygen therapy.[13] In agreement with the study by Wing *et al*., demonstrated the reduction of intubation rate after implementation HFNC guideline compared to the period before the availability of HFNC (odds ratio 0.17; 95% CI 0.06–0.50; $P = 0.001$).[16]

Most children in HFNC therapy group had a significant reduction in RR, HR at 120 and 360 min compared with conventional oxygen therapy. Although children in HFNC group had higher baseline clinical respiratory score, they had a significant reduction in respiratory scores at 240 min after applying HFNC treatment. This effect, however, could explain by various potential mechanisms of HFNC. It can reduce work of breathing by decreasing dead space, increasing mucociliary clearance, and minimal increasing distending pressure.[6,7]

We also found that children who failed HFNC therapy had higher respiratory score at 60 min compared to the successful group. In agreement with the previous study of McKiernan *et al*., revealed that children who required intubation after 60 min of HFNC had less reduction in RR (1 ± 17 bpm) compared to infants who did not require intubation (14 ± 15 bpm).[11] Schibler *et al*. also described infants who had a 20% reduction in RR and HR after 90 min of intervention did not require intubation while on HFNC.[14] Nevertheless, there were some limitations in our study such as our study could not be blinded and inter-rater reliability.

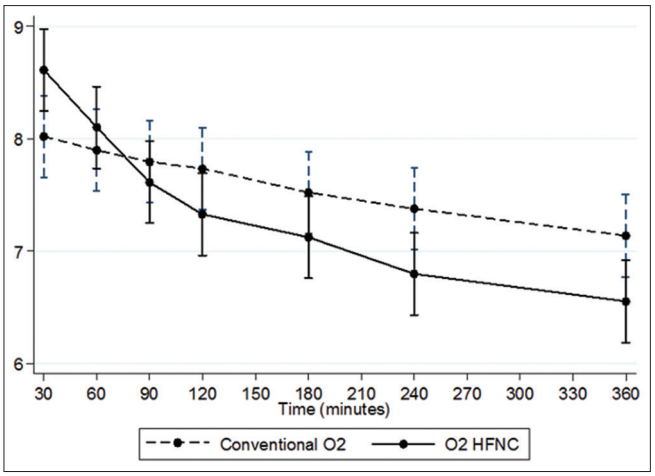

Figure 3: Graph shows respiratory score after the treatment compare between high flow nasal cannula and conventional group

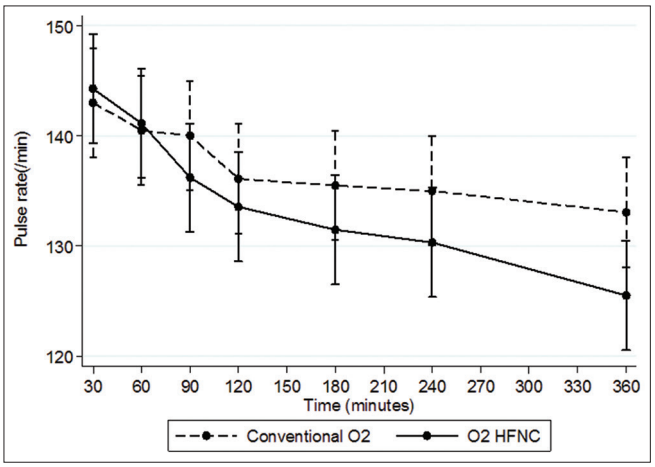

Figure 4: Graph compare pulse rate between high flow nasal cannula and conventional group after the treatment

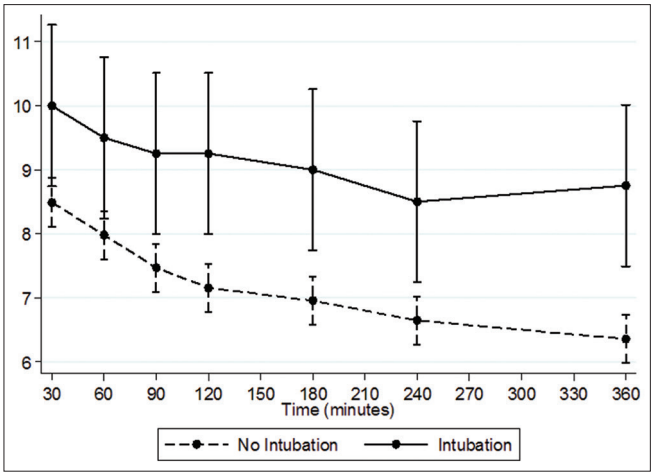

Figure 5: Graph compares respiratory score between failed and success group in children who treated with high-flow nasal cannula

Conclusion

This study revealed that HFNC therapy had a potential clinical advantage in the management of children hospitalized with respiratory distress compared with conventional oxygen therapy. The early use of HFNC therapy in children with moderate-to-severe respiratory distress may prevent endotracheal intubation. Respiratory score, RR, and HR should be closely monitored. If there is no clinical improvement or worsening, step up treatment to NIPPV or intubation should not be delayed.

Financial support and sponsorship

Ratchada Pisek Sompotch Fund.

Conflicts of interest

There are no conflicts of interest.

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