Original Article

High-Flow Nasal Cannula versus Conventional Oxygen Therapy in Post-Extubation Pediatric Patients: A Randomized Controlled Trial

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Objective: To compare the extubation failure in high-flow nasal cannula [HFNC] group versus conventional oxygen therapy [COT] group in pediatric intensive care unit [PICU] patients after extubation.

Materials and Methods: The present research conducted a randomized, controlled trial in children aged 29 days to 15 years admitted to PICU, Maharat Nakhon Ratchasima Hospital, between August 1, 2016 and May 31, 2017. The patients were clinically ready for extubation after received mechanical ventilation for at least 24 hours, and were randomly allocated to HFNC or COT groups.

Results: One hundred fifty-two patients were enrolled (76 patients in each group). Extubation failure in HFNC and COT group were 11.8% and 14.5% ($p = 0.81$), respectively. In COT group, higher incidence of extubation failure was observed in patients aged less than one year (6.6% versus 2.6%) and mechanically ventilated time greater than seven days (2.6% versus 0). There was more atelectasis after extubation in COT group than HFNC group (15.8% versus 6.6%, $p = 0.12$).

Conclusion: The present study showed no statistical differences in extubation failure and adverse effects between the two groups, but there was decreasing tendency of failure and atelectasis in the HFNC group.

Keywords: Extubation failure, High flow nasal cannula, Post-extubation, Pediatrics

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Extubation failure is a common problem for ventilated-patients in pediatric intensive care unit [PICU]. Several oxygen devices have been used to support recently weaned patients and reduce extubation failure[1]. Partial rebreathing mask has been commonly used in PICU. Disadvantages of this device are unstable fraction of inspired oxygen [FiO_2], uncomfortable, mask displacement, difficult to eat or speak, aspiration, and skin irritation[2,3]. Currently, a high-flow nasal cannula [HFNC] is increasingly used for post-extubation respiratory support. This device delivers a high total flow that is sufficient to patient's inspiratory demand including constant FiO_2[4]. HFNC reduces work of breathing, improves alveolar ventilation, improves secretion clearance, produces positive distending pressure, and is comfortable[4,5].

In preterm infants, HFNC is used in respiratory distress syndrome, apnea of prematurity, and post-extubation respiratory support[4,6-8]. In pediatrics, HFNC is used in acute bronchiolitis, viral-induced wheeze, asthma, pneumonia, viral croup, obstructive sleep apnea, post-extubation stridor, cardiomyopathy, acute pulmonary edema, post-extubation respiratory support, and inter-hospital transport of critically ill patients[4,5,9,10]. There are several clinical studies of HFNC as a post-extubation respiratory support in preterm infants and in adult population but only a few studies in children[4,6-8,10-17]. The purpose of the present study was to compare the extubation failure in HFNC group versus conventional oxygen therapy [COT] group in PICU patients after extubation.

Materials and Methods

The present study was a randomized, controlled trial, approved by the Institutional Review Board of Maharat Nakhon Ratchasima Hospital and written informed consents were obtained from parents or guardians. Children aged 29 days to 15 years admitted to an 8-bed PICU, Department of Pediatrics, Maharat Nakhon Ratchasima Hospital between August 1, 2016 and May 31, 2017 and received mechanical ventilation for at least 24 hours were eligible for the present study. Patients were recruited and assessed by the attending physicians, when clinically ready for

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extubation[18]. Exclusion criteria were neuromuscular disease, tracheostomy, air-leak syndrome, planned use of non-invasive ventilation [NIV] after extubation, unplanned extubation, previous recruitment, and nasal abnormalities.

Patients were randomly allocated to HFNC or COT groups. Randomization was computerized generated. The attending physicians opened sequentially numbered, sealed opaque envelopes immediately before extubation.

HFNC (Optiflow junior, OPT 316 & 318, Optiflow tubing kit, RT 330, Fisher & Paykel Healthcare Ltd., New Zealand) was applied to patients in HFNC group immediately after extubation. Total flow was initially set at 1 L/kg/minute and titrated until optimized breath sound. FiO_2 was initially set as FiO_2 while on the ventilator and adjusted to maintain oxygen saturation [SpO_2] of at least 94%. Temperature of heated humidifier (MR 730 & 850, Fisher & Paykel Healthcare Ltd., New Zealand) was set at 37°C. COT was applied through partial rebreathing mask at oxygen flow rate 10 L/minute to maintain SpO_2 of at least 94%. Patients in both groups were treated by the same medical and nursing staffs and received similar medical management. The device was applied for at least 24 hours or until clinical improvement. The cessation of oxygen therapy was judged by the attending physicians.

Body temperature, pulse rate, respiratory rate, and blood pressure before extubation and 30 minutes after applied oxygen device were recorded by PICU nurses. Blood gas analysis was checked before extubation and 60 minutes after applied oxygen device. Chest radiography was done within 12 hours after applied oxygen device. Cause of extubation failure, time to extubation failure, mortality, and adverse effects were recorded and summarized by the investigator.

The primary outcome was extubation failure, defined as the need for reintubation or NIV within 48 hours after extubation[10,13,18-20]. Causes of extubation failure included respiratory distress, hypoxemia, hypercapnia with respiratory acidosis, decreased level of consciousness, upper airway obstruction, apnea, and cardiovascular instability[13,20,21]. Proper respiratory support after extubation failure depended on the attending physicians. Secondary outcome were mortality and adverse effects of device. Adverse effects included nasal ulcer, pressure sore, abdominal distension, atelectasis, and pneumothorax.

Based on a previous study, the extubation failure rate was used to calculate the sample size[10]. The present study recruited various cause of acute respiratory failure, then the authors estimated the reduction of extubation failure rate from 20% in COT group to 5% in HFNC group. With an alpha error of 0.05 and a power of 80%, the sample size was of 152 patients (76 patients in each group).

Categorical variables were compared by Chi-square or Fisher's exact test. Continuous variables were compared by independent sample t-test. A *p*-value less than 0.05 was statistically significant. Kaplan-Meier curves were plotted to assess the time from extubation to reintubation between the two groups and compared by the log-rank test. Statistical analyses of the results were done with StataCorp Stata 14.

Results

During the study period, 256 patients were eligible, and 104 patients were excluded from the study. One hundred fifty-two patients were enrolled (Figure 1). Demographic and clinical characteristics of patients were similar between the two groups (Table 1).

Extubation failure was found in 9 patients (11.8%) in HFNC and 11 patients (14.5%) in COT

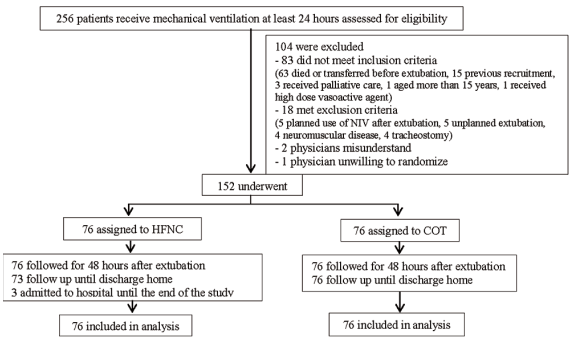

Figure 1. Participant flow diagram.

Table 1. Patient baseline characteristics

Characteristic	HFNC group (n = 76)	COT group (n = 76)
Male, n (%)	49 (64.5)	58 (76.3)
Age (months), mean ± SD	42.6±49.2	32±39.1
Body weight (kg), mean ± SD	13.7±10.8	12.1±9.2
Underlying disease, n (%)	39 (51.3)	30 (39.5)
Cause of acute respiratory failure, n (%)		
Respiratory primary failure	56 (73.7)	61 (80.3)
Post-operative state	12 (15.8)	10 (13.1)
Neurologic dysfunction	8 (10.5)	5 (6.6)
Length of mechanical ventilation before extubation (days), mean ± SD	5.6±8.9	4.7±6.4
Corticosteroid usage before extubation, n (%)	17 (22.4)	19 (25.0)

HFNC = high-flow nasal cannula; COT = conventional oxygen therapy

group. There was no statistical difference between the two groups (p = 0.81). All patients with extubation failure required reintubation. Most common cause of extubation failure in both groups was upper airway obstruction (Table 2). Extubation failure was most likely to occur within 12 hours after extubation in both groups (Figure 2). In COT group, higher incidence of extubation failure was observed in patients aged less than one year (6.6% versus 2.6%) and mechanically ventilated time greater than seven days (2.6% versus 0%).

There was more atelectasis after extubation in COT group than HFNC group (15.8% versus 6.6%) but no statistical difference. There was no other adverse effect e.g., nasal ulcer, pressure sore, abdominal distension, and pneumothorax in either group. Mortality rate, length of hospital stays, length of PICU stay, length of oxygen therapy, and corticosteroid use were similar, with no statistical difference between the two groups (Table 3).

Discussion

Several clinical studies were done on the use HFNC as a post-extubation respiratory support[4,6-8,10-17]. In the present study, a randomized controlled trial was conducted to evaluate efficacy of HFNC in post-extubation pediatric patients in Thailand.

There was no statistical difference (p = 0.81) in extubation failure rate in HFNC and COT but there was a tendency to be lower in HFNC group (11.8% versus 14.5%). Previous studies compared the efficacy between HFNC and COT in post-extubation adult patients and showed that extubation failure was significantly lowered in the HFNC group, which is consistent with Testa's study in pediatric cardiac surgical patients after extubation[10,14,17]. The higher incidence of extubation failure in HFNC group of the present study was probably attributed to various causes of acute respiratory failure and various ages. In COT group, higher incidence of extubation failure was observed in patients aged less than one year (6.6% versus 2.6%) and mechanically ventilated time greater than seven days (2.6% versus 0%).

Causes of extubation failure were not statistically different between the two groups (p = 0.81). The most common cause of extubation failure in the present study was respiratory in both groups, and upper airway obstruction was the leading cause, which is different from Hernandez et al[17].

Atelectasis after extubation was a tendency to be lower in HFNC group but with no statistical difference

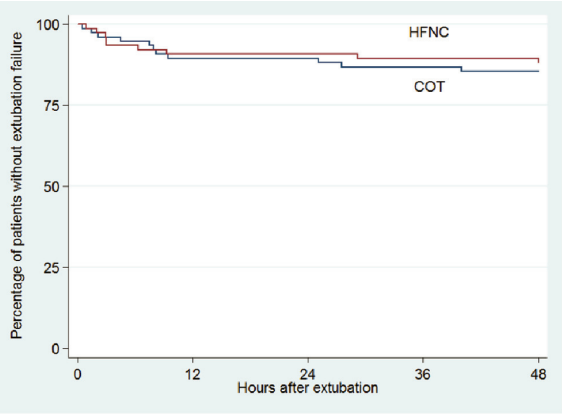

Figure 2. Patients without extubation failure after extubation.

Table 2. Primary outcome

Outcome	HFNC group (n = 76)	COT group (n = 76)	p-value
Extubation failure within 48 hours, n (%)	9 (11.8)	11 (14.5)	0.81
Age <1 year, n (%)	2 (2.6)	5 (6.6)	0.42
Duration of mechanical ventilation before extubation >7 days, n (%)	0 (0.0)	2 (2.6)	0.48
Cause of extubation failure, n (%)			0.81
Respiratory distress	1 (11.1)	0 (0.0)	
Hypoxemia	2 (22.2)	4 (36.4)	
Decreased level of conciousness	1 (11.1)	0 (0.0)	
Upper airway obstruction	4 (44.4)	6 (54.5)	
Apnea	1 (11.1)	1 (9.1)	
Time to reintubation (hours), mean ± SD	11.6±16.2	12.2±12.8	0.93

HFNC = high-flow nasal cannula; COT = conventional oxygen therapy

Table 3. Secondary and other outcomes

Outcome	HFNC group (n = 76)	COT group (n = 76)	p-value
Adverse effects, n (%)			0.12
Atelectasis	5 (6.6)	12 (15.8)	
Other	0 (0.0)	0 (0.0)	
Death, n (%)	4 (5.3)	3 (3.9)	1.0
Length of oxygen therapy after extubation (days), mean ± SD	5.3±6.9	4.3±5.8	0.3
Length of hospital stay (days), mean ± SD	26.5±41.6	17.5±15.3	0.07
Length of PICU stay (days), mean ± SD	8.1±10.3	6.7±7.2	0.3
Corticosteroid usage after extubation, n (%)	22 (28.9)	29 (38.2)	0.3

HFNC = high-flow nasal cannula; COT = conventional oxygen therapy; PICU = pediatric intensive care unit

(6.6% versus 15.8%, $p = 0.12$), which differed from previous studies[10,12]. There was no other adverse effect such as nasal ulcer, abdominal distension, and pneumothorax. This confirmed safety to use of HFNC, which is similar to Hernandez et al[17]. Testa et al's study showed pneumothorax, pleural effusion, and abdominal distension in HFNC[10]. However, another study found a significantly fewer adverse effect in HFNC[13,16].

In the present study, there was no statistical difference in mortality rate, length of oxygen therapy after extubation, length of hospital stays, length of PICU stay, and corticosteroid usage after extubation between the two groups. This is in line with other studies[10,14,17].

There are some limitations in the present study. First, patients and attending personnel could not be blinded to the treatment but these personnel were not involved in the project. Second, the decision to extubation and extubation failure depended on clinical judgement by the attending physicians. And third, the period of PICU observation after extubation was short because of the overcrowding in the PICU.

Conclusion

There was no statistical difference in extubation failure between HFNC and COT group in post-extubation pediatric patients. HFNC may be effective in young-age patients and longer duration of mechanical ventilation. There were no significant adverse effects in both groups, but incidence of atelectasis was lower in the HFNC group.

What is already known on this topic?

HFNC is increasingly used in preterm infants, children, and adults. Several clinical studies of HFNC as a post-extubation respiratory support in preterm infants and in adult population have been done but only a few studies in children.

What this study adds?

There is no difference in extubation failure and adverse effects between HFNC and COT in post-extubation pediatric patients, but HFNC may be more effective in young-age and longer duration of mechanical ventilation patients.

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Potential conflicts of interest

The authors declare no conflict of interest.

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