Acta Med. Okayama, 2019
Vol. 73, No. 1, pp. 15–20
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Acta Medica Okayama
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Original Article

High-flow Nasal Cannula Versus Noninvasive ventilation for Postextubation Acute Respiratory Failure after Pediatric Cardiac Surgery

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We compared the reintubation rate in children who received high-flow nasal cannula (HFNC) therapy to the rate in children who received noninvasive ventilation (NIV) therapy for acute respiratory failure (ARF) after cardiac surgery. This was a retrospective analysis of 35 children who received HFNC therapy for ARF after cardiac surgery in 2014-2015 (the HFNC group). We selected 35 children who had received NIV therapy for ARF after cardiac surgery in 2009-2012 as a control group. The matching parameters were body weight and risk adjustment for congenital heart surgery category 1. The reintubation rate within 48 h in the HFNC group tended to be lower than that in the NIV group (3% vs. 17%, $p = 0.06$). The reintubation rate within 28 days was significantly lower in the HFNC group compared to the NIV group (3% vs. 26%, $p = 0.04$). The HFNC group's ICU stays were significantly shorter than those of the NIV group: 10 (IQR: 7-17) days vs. 17 (11-32) days, $p = 0.009$. HFNC therapy might be associated with a reduced reintubation rate in children with ARF after cardiac surgery.

Key words: high-flow nasal cannula, noninvasive ventilation, reintubation, congenital heart disease, acute respiratory failure

The rates of reintubation after pediatric and neonatal cardiac surgery are approx. 6-9% and 17%, respectively [1-3]. Unsuccessful extubation is associated with a long intensive care unit (ICU) length of stay (LOS) and a high rate of mortality [1,2]. Therefore, adequate respiratory support to prevent the need for reintubation is crucial. Noninvasive ventilation (NIV) therapy has been used as a respiratory support in children over the past few years [4,5]. At our institute, NIV is used as the first-line therapy for respiratory support after pediatric cardiac surgery to avoid intubation, because NIV is less invasive compared to mechanical ventilation with intubation.

A high-flow nasal cannula (HFNC) is a respiratory support device that can deliver heated and humidified gas at a high flow rate [6]. It can provide precise fractional oxygen delivery, mild positive airway pressure, washout of nasopharyngeal dead space, and a reduction of airway resistance [4,5,7,8]. HFNC has advantages over NIV therapy, such as ease of use and better patient's comfort [9]. In adult subjects in a randomized controlled trial (RCT), the use of HFNC therapy was associated with a lower rate of reintubation compared to that of conventional oxygen therapy [10].

NIV therapy for children is sometimes difficult because of the patients' limited compliance and cooperation; thus, the use of HFNC as an alternative to NIV therapy for respiratory support in children is increasing. However, only a few RCTs have compared HFNC

Received July 6, 2018; accepted October 19, 2018.
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Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

therapy with NIV therapy in children [11, 12]. There has been no study in which the reintubation rate in patients receiving HFNC therapy was compared to that in patients receiving NIV therapy after pediatric cardiac surgery.

We hypothesized that the reintubation rate would be lower in patients receiving HFNC therapy compared to patients receiving NIV therapy. The primary outcome of the present study was the reintubation rate within 48 h after the diagnosis of acute respiratory failure (ARF) in a comparison of HFNC and NIV groups.

Patients and Methods

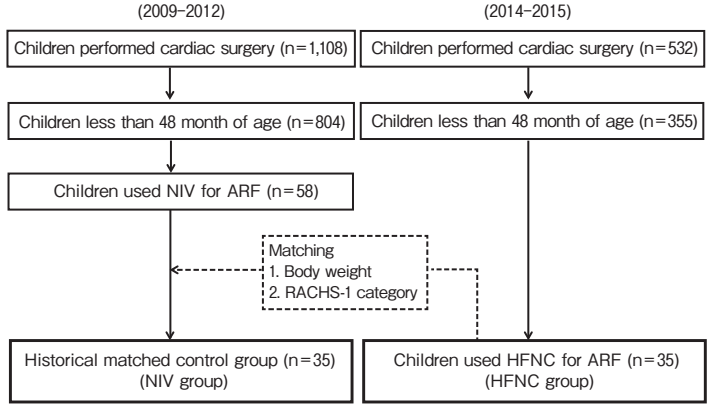
Setting. This study was conducted in a tertiary teaching hospital that has 865 beds including 8 beds in the pediatric cardiac ICU.

Design and patients. The study was a retrospective matched-control before-after study. The Institutional Review Board (IRB) of Okayama University Hospital approved the study (no. 1602-505). The IRB did not require individual patient's written informed consent because of the retrospective study design. Children aged < 48 months who had received HFNC or NIV therapy for ARF after pediatric cardiac surgery were included in the study. HFNC therapy was first used in our pediatric cardiac ICU in 2013. After the introduction of HFNC therapy, the use of NIV therapy was replaced by HFNC therapy, and NIV therapy was used only as a bridging therapy to reintubation if HFNC therapy was not effective.

Fig. 1 provides the case selection flowchart. The HFNC group was the 35 patients who received HFNC therapy during the 2-year period from January 2014 to December 2015. We collected the cases of 35 other patients as a matched control group who had received NIV therapy after pediatric cardiac surgery during the 4-year period from January 2009 to December 2012 (the NIV group). The matching parameters were body weight (within 3 kg) and risk adjustment for congenital heart surgery category 1 (RACHS-1) [13] (less than category 2), which represents the complexity of the pediatric surgery. Matching priority was given to body weight.

Definition of ARF and methods used for NIV therapy and HFNC therapy. The definition of ARF is given in Table 1. In our practice, HFNC (Optiflow; Fisher and Paykel Healthcare, Auckland, New Zealand) was performed immediately after the diagnosis of postextubation ARF. Flow was commenced at 2 L/kg/min. The fraction of inspiratory oxygen (F_IO_2) was set to achieve target oxygen saturation (total repair, > 92%; palliative operation, 75-85%). The temperature of gas was set to 37°C with a humidifier. We selected the nasal cannula size according to the child's weight and nasal size.

In our practice, NIV therapy was also performed immediately after a diagnosis of postextubation ARF. NIV was delivered by using a fixed tracheal tube as a nasal prong, which was inserted nasally and positioned



HFNC high flow nasal cannula, NIV non invasive ventilation, ARF acute respiratory failure
RACHS-1 Risk adjustment for congenital heart surgery 1

Fig. 1 The 35 patients who received HFNC therapy during the period from January 2014 to December 2015 at our institute were the HFNC group. For the matched control group, we collected the cases of 35 patients who had received NIV therapy after pediatric cardiac surgery from January 2009 to December 2012. The matching parameters were body weight and RACHS-1 category.

Table 1 Definition of ARF

Tachypnea	RR > 50 breath per min (< 1 year old) RR > 40 breath per min (1–4 years old)
Hypoxemia	SaO_2 < 92% (Total repair) SaO_2 < 75% (Palliative operation)
Hypercapnia	$PaCO_2$ > 50 mmHg
Increased work of breathing	Using accessory respiratory muscle

ARF is defined by at least one of the criteria.
ARF, acute respiratory failure; RR, respiratory rate; SaO_2, saturation of arterial oxygen; $PaCO_2$, partial pressure of arterial carbon dioxide.

just before the vocal cord. Continuous positive airway pressure (CPAP) was delivered by using a ventilator (Servo I, MAQUET Holding, Rastat, Germany). The F_IO_2 was set to achieve target oxygen saturation (total repair, >92%; palliative operation, 75-85%). The CPAP was set to 10 cmH_2O.

If failure occurred with these treatments, NIV therapy or tracheal intubation and invasive mechanical ventilation were initiated based on the clinical judgment of the physician. Treating physicians conducted reintubation on the basis of clinical signs: increased respiratory rate, worsening gas exchange, and patient intolerance. These criteria for reintubation were unchanged during the two study periods.

Data collection. We collected the patients' data from their electronic healthcare records including data for age, body weight, gender, RACHS-1 category, baseline vital signs, reintubation rates within 48 h and within 28 days after the diagnosis of ARF, and the ICU LOS.

The duration of mechanical ventilation was defined as the period since the commencement of mechanical ventilation after cardiac surgery until extubation. The attending physician decided the uses of sedative drugs in both the NIV and HFNC groups according to the patient's condition.

Statistical analysis. Continuous data are expressed as medians and their interquartile range (IQR) when the data had a non-normal distribution. Categorical data are presented as percentages. McNemar's test was used to compare reintubation rates within 48 h and within 28 days after the diagnosis of ARF, and the Wilcoxon signed-rank test was used for the ICU LOS data. We used a logistic regression model to adjust for the patient age to investigate the risk of reintubation within 48 h and 28 days between the NIV and HFNC groups. Two-tailed p-values <0.05 were considered significant. All statistical analyses were performed using statistical software (JMP® ver. 12; SAS, Cary, NC, USA).

Results

Patient population. Table 2 summarizes the clinical characteristics and baseline vital signs of the children in the HFNC group and NIV group. There was no significant difference between the two groups in body weight, RACHS-1 category, duration of mechanical ventilation, or baseline vital signs. The patients in the HFNC group were significantly younger (median 3 months, IQR 1.0-9.0) than those in the NIV group (median 1 months, IQR 0-5.0) ($p=0.01$). The median settings of the HFNC group were F_IO_2 of 0.5 (IQR: 0.3-0.52) and flow rate of 2.1 (1.7-2.3) L/kg/min, and those of the NIV group were F_IO_2 of 0.5 (0.21-0.8) and CPAP of 10 (8-10) cmH_2O.

The percentage of sedative drug use in the HFNC group was 49% (dexmedetomidine 37%, dexmedetomidine + morphine 6%, morphine 3%, and fentanyl 3%) and that in the NIV group was 49% (dexmedetomidine 20%, morphine 23%, dexmedetomidine + fentanyl 3%, and dexmedetomidine + midazolam 3%) ($p=0.81$).

Outcomes. Table 3 shows the results of the univariate analysis of the outcome data of the HFNC and NIV groups. The reintubation rate within 48 h after the diagnosis of ARF in the HFNC group tended to be lower than that in the NIV group (3% vs. 17%, $p=0.06$), but not significantly so. We performed a logistic regression to adjust for the age difference between the two groups, and the results revealed that HFNC therapy was an independent negative predictor for reintubation within 48 h: adjusted odds ratio (95% confidence interval) 0.08 (0.002-0.6), $p=0.01$. The reasons for reintubation within 48 h after the diagnosis of ARF were cardiac and respiratory support (n = 1) in the HFNC group and cardiac and respiratory support (n = 3) and respiratory support (n = 3) in the NIV group. Reintubation was performed after bridging with NIV therapy in one patient in the HFNC group.

The reintubation rate within 28 days after the diagnosis of ARF was significantly lower in the HFNC group compared to the NIV group (3% vs. 26%, $p=0.04$). The

Table 2 Main clinical characteristics and baseline vital signs of the HFNC and NIV groups

Variables	HFNC group (n = 35)	NIV group (n = 35)	*p* Value
Body weight (kg, IQR)	3.9 (2.9–5.5)	3.4 (2.7–4.8)	0.14
RACHS-1 category	3 (2–4)	3 (3–4)	0.09
Age (months, IQR)	3 (1.0–9.0)	1 (0–5.0)	0.01
MV time (h, IQR)	75 (7–171)	93.5 (40–242)	0.23
Palliative surgery (%)	40	51	0.33
CPB (%)	80	82	0.75
CPB time (h, IQR)	110 (69–137)	119 (81–153)	0.37
Operative time (min, IQR)	192 (126–243)	216 (167–285)	0.31
Blood loss (ml, IQR)	18 (0–38)	30 (5–50)	0.14
Duration of HFNC (h, IQR)	43 (20–64)	–	–
Duration of NIV (h, IQR)	–	38 (22–72)	–
Time to diagnosis of ARF after extubation (h, IQR)	4 (0–4)	3.5 (0–4)	0.49
RR (breaths/min, IQR)	43 (33–55)	39 (32–50)	0.47
$PaCO_2$ (mmHg, IQR)	45.7 (40.1–53.2)	49.1 (44.6–56.1)	0.16
SaO_2 (%, IQR)	89.9 (76.9–96.4)	81.2 (70.4–97.0)	0.36
SBP (mmHg, IQR)	87 (78–98)	86 (75–100)	0.55
HR (bpm, IQR)	141 (119–155)	142 (132–160)	0.16

HFNC, high-flow nasal cannula; NIV, noninvasive ventilation; IQR, interquartile range; RACHS-1, Risk adjustment for congenital heart surgery 1; MV, Mechanical ventilation; CPB, cardiopulmonary bypass; RR, respiratory rate; $PaCO_2$, partial pressure of arterial carbon dioxide; SaO_2, arterial oxygen saturation; SBP, systolic blood pressure; HR, heart rate.

Table 3 Univariate analysis of outcome data

Outcomes		HFNC group (n = 35)	NIV group (n = 35)	*p* Value
Reintubation within 48 h	n (%)	1 (3)	6 (17)	0.06
Reintubation within 28 days	n (%)	1 (3)	9 (26)	0.04
ICU LOS (days, IQR)		10 (7–17)	17 (11–32)	0.009

HFNC, high-flow nasal cannula; NIV, noninvasive ventilation; IQR, interquartile range; LOS, length of stay.

Table 4 Logistic regression of outcome data

Variable	OR	Lower 95% CI	Upper 95% CI	*p* Value
48 h reintubation rate				
HFNC	0.08	0.003	0.63	0.01
Age	0.93	0.85	1.01	0.06
28 days reintubation rate				
HFNC	0.08	0.006	0.98	0.04
Age	0.93	0.86	1.00	0.06

OR, odds ration; CI, confidential interval; HFNC, high flow nasal cannula.

reasons for reintubation between 48 h and 28 days after the ARF diagnosis in the NIV group were cardiac and respiratory support (n = 2) and diaphragmatic paralysis (n = 1).

Table 4 lists the results of the logistic regression. After adjustment of age, HFNC therapy was an independent negative predictor for reintubation within both 48 h and 28 days.

The ICU LOS in the HFNC group (median 10 days, IQR 7-17 days) was significantly shorter than that in the NIV group (median 17 days, IQR 11-32 days, $p = 0.009$).

Discussion

This is the first study to compare the rate of reintubation after the diagnosis of ARF in patients receiving NIV therapy to that in patients receiving HFNC therapy for postextubation ARF after pediatric cardiac surgery. The results of a univariate analysis demonstrated that although the reintubation rate within 48 h after the diagnosis of ARF was not significantly different between the HFNC and NIV groups, the reintubation rate within 28 days after the ARF diagnosis was significantly lower in the HFNC group compared to the NIV group.

In the NIV group, the reintubation rates within 48 h and within 28 days after the diagnosis of ARF were 17% and 26%, respectively. In past studies, the reintubation rates in patients who received NIV therapy ranged from 20% to 35% [14-16]. The rate of reintubation in the patients who received NIV therapy in our study is similar to these reported rates.

The rate of reintubation within 28 days after the ARF diagnosis was low in the present HFNC group. This might be due to differences in the characteristics of the devices used in the two groups. A previous study estimated that the positive pressure delivered by HFNC therapy (2 L/kg/min) was 4-6 cmH_2O [17]. HFNC also provides a wash-out of anatomical dead space and then reduces the work of breathing. The CPAP level in our NIV group was 10 cmH_2O. However, NIV increases dead space. To compensate for the increased dead space, more minute ventilation will be needed and this will increase the work of breathing. These differences might have caused the difference in the rate of reintubation between the present HFNC and NIV groups.

Two retrospective studies showed that HFNC therapy might reduce the need for intubation in infants with bronchiolitis and children with respiratory distress [18, 19]. Our present finding that HFNC therapy was associated with a low reintubation rate is concordant with the results of those studies. In addition, our previous study demonstrated a beneficial physiological impact of HFNC on patients with ARF after pediatric surgery [20]. We thus hypothesized that HFNC could prevent ARF after pediatric cardiac surgery, and an intervention study is now underway at our institute [21].

Limitations. This was a retrospective study. We compared the rate of reintubation in the HFNC group to that in a historical control NIV group. However, our clinical methods for respiratory support and reintubation did not change during the two study periods. In addition, we included patients with different characteristics and conditions (age, cyanosis, type of operation). We therefore matched the body weight and RACHS-1 category between the 2 groups. This process could reduce the issues related to different patient populations, but there might be unmatched baseline differences after the matching process which might have affected our results. Among these baseline differences, age was associated with reintubation after pediatric surgery in another study [22]. We thus conducted a post hoc adjustment of age difference between the two groups using a logistic method. The results showed that HFNC therapy was still an independent negative predictor after the adjustment for patient age.

The NIV method using a fixed tracheal tube as a nasal prong [23] is not commonly used compared to the mask method, and thus the generalization of our results is limited.

In conclusion, HFNC might be associated with a low rate of reintubation in children with ARF after cardiac surgery.

Acknowledgments. This study was supported by grants-in-aid for scientific research from the Ministry of Education, Science, and Culture of Japan: MEXT/JSPS KAKENHI grant no. JP26861233.

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