ORIGINAL ARTICLE

The Weaning Protocol of High Flow Nasal Cannula Reduce Duration of Weaning in Lower-Respiratory Tract Infection in Children Who Used High Flow Nasal Cannula: Single Center Experience in Thailand

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Background: Use of high flow nasal cannula (HFNC) has been widely accepted as non-invasive respiratory support in children suffering from lower respiratory tract infections (LRI). Patients who use HFNC still need respiratory care from health personnel in ICU or intermediate care wards. Without the weaning protocol, the authors had noticed prolonged HFNC use, which affected the length of hospital stay (LOS). As such, a pediatric patient care team (PCT) created the weaning protocol and collected data whether the weaning protocol would shorten weaning time.

Objective: To compare HFNC weaning times among children suffering from LRI, before and after using the weaning protocol.

Materials and Methods: A pre- and post-intervention study of 1-month-old to 5-year-old children who received HFNC therapy for LRI at Panyananthaphikkhu Chonprathan Medical Center between August 2018 and July 2020, the one year before and after the protocol was implemented in August 2019, were carried out. Demographic data and severity of respiratory illness according to Respiratory Assessment Score (RAS) were recorded. Multivariate linear regression, adjusted for age, gender, weight, RR, HR, SpO_2, and RAS before using HFNC, was used to compare between the pre- and post-weaning protocol groups according to total HFNC time, duration of weaning time, and LOS.

Results: There were 25 patients in each group. The mean age in the post-weaning protocol group was lower, but there was no difference in severity. Multivariate linear regression demonstrated that the post-weaning protocol group had a significantly shorter weaning time at 49.5±37.0 hours versus 84.2±62.8 hours (p=0.034). Moreover, total HFNC time was also significantly shorter in the post-weaning protocol group at 71.53±36.7 hours versus 119.6±78.2 hours (p=0.019). There was no difference in vital signs during weaning between the two groups.

Conclusion: Implementing the weaning protocol reduce weaning time and total HFNC time, without affecting clinical outcomes.

Keywords: High flow nasal cannula; Weaning protocol; Lower respiratory tract infection; Length of stay

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High flow nasal cannula (HFNC) was initially used in newborns as non-invasive respiratory support to provide continuous positive airway pressure (CPAP)[1]. Recently, HFNC has been widely used beyond the newborn period[2-5]. In pediatrics departments, HFNC use was first introduced to treat young children with moderate bronchiolitis[6,7], but there has been an increasing trend to use it in other indications, such as lower respiratory tract infection[8-13] and post-extubation[5] as the interface is well tolerated by pediatrics patients[3,14].

HFNC can decrease the work of breathing in patients because it delivers a heated and humidified mixture of air and oxygen at a flow higher than the patients' inspiratory flow[15]. A flow higher than the patients' inspiratory flow can create positive pharyngeal pressure and wash out the end-expiratory oxygen-depleted gas[9]. A previous study measured pharyngeal pressure throughout a gradual increase in flow in children with bronchiolitis and showed a flow of at least 6 L/minute could create positive inspiratory and expiratory pharyngeal pressure[6,14], but the positive pharyngeal pressure seemed to plateau at a flow over 2 L/kg/minute. Moreover, HFNC provides warm gas at 34 to 37°C, at a humidity of nearly 100%, which enhances mucociliary function[15]. In the

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authors' practice, a flow rate of at least 6 L/minute was determined as high flow and a flow rate of 2 L/kg/minute was the maximum starting flow[16].

Although HFNC is a simple interface and more tolerable for pediatric patients, close monitoring is also important. In the present study setting, HFNC was commonly used in children with lower respiratory tract infections such as bronchiolitis, bronchitis, and pneumonia. The staff and nurses could initially set the HFNC proficiently, with an initial flow of at least 6 L/minute but not more than 2 L/kg/minute, but they were uncomfortable on weaning the flow rate. The use of HFNC seemed to prolong the length of stay in patients with lower respiratory tract infections who used HFNC. The patient care team (PCT) of the Pediatrics Department of Panyananthaphikkhu Chonprathan Medical Center implemented the weaning protocol of HFNC in August 2019. It was observed that the weaning protocol reduced the duration of weaning time in this group. Therefore, the purpose of the present routine research study was to define the effect of using the weaning protocol to reduce the duration of weaning time. A secondary objective was to compare the patients' conditions during the weaning for respiratory rate (RR), heart rate (HR), and oxygen saturation (SpO_2) and the length of hospital stay (LOS) between pre- and post-implementation of the weaning protocol.

Materials and Methods

The present study was a pre- and post-intervention study of children who received HFNC therapy for lower respiratory tract infection at Panyananthaphikkhu Chonprathan Medical Center between August 2018 and July 2020. In August 2019, the weaning protocol for HFNC was implemented in the Pediatrics Department. The pre-protocol cohort comprised patients seen between August 2018 and July 2019, and the post-protocol cohort comprised patients seen between August 2019 and July 2020. The pilot data from the PCT of the Pediatrics Department showed the duration of weaning in pre- and post-weaning protocol were 120 and 70 hours, respectively. Therefore, the sample size of at least 25 in each group was calculated by testing two independent means in Stata®. Age under two years old, and diagnosis and severity of disease before use of HFNC were identified as confounding factors and were matched between groups.

All data was collected from the electronic medical records. Fifty children, aged one month to five years old who received HFNC therapy for lower respiratory tract infection were included. Children having chronic respiratory problems such as bronchopulmonary dysplasia, chronic aspiration syndrome, congenital heart disease with heart failure, and congenital lung anomalies were excluded. HFNC-treated patients were admitted to the pediatric intensive care unit (PICU) or the intermediate care units where they were managed by pediatric critical care physicians and residents. The patients received respiratory therapy provided by nursing staff.

Approval to conduct the study was obtained from the Ethics Committee of the Panyananthaphikkhu Chonprathan Medical Center (EC number 022/62).

HFNC weaning protocol

The HFNC weaning Protocol was created by referring to the "HFNC Holiday Protocol"[1]. The present study weaning protocol used the Respiratory Assessment Score (RAS) to assess the severity of patients as the holiday protocol did. RAS scores assess RR, severity of chest retraction by chest movement, intercostal retraction, and xiphoid retraction, nasal flaring, and grunting. The authors also evaluated RR, HR, and SpO_2 before and after using HFNC. RAS was used to match severity of the patients' conditions in both the pre-and post-protocol group.

The authors assessed the patients' respiratory status (RR, HR, SpO_2 and respiratory effort) every eight hours as per the duty shifts of staff. Pediatric critical care physicians and residents could decide to start weaning at any time. Patients with clinical improvement (decreased respiratory effort, decreased RR, and decreased HR) had their HFNC flow decreased by half every eight hours. The patients whom physicians considered not ready to wean or had shown no improvement remained in the current settings and were reassessed during the next eight hours.

Failure of the protocol was defined as failure to decrease the high flow rate as decided after clinical status was improved.

Statistical analysis

Statistical analysis was performed using Stata, version 14 (StataCorp LP, College Station, TX, USA). Descriptive statistics were reported for all variables of interest as mean ± standard deviations or median and interquartile ranges for continuous measurements, or counts and percentages for categorical data, as appropriated. Mean levels of duration parameters such as duration of weaning (duration of time using HFNC, and LOS) and clinical parameters during

Table 1. Baseline characteristics of children who use HFNC (n=50)

Variables	Post-weaning protocol group (n=25)	Pre-weaning protocol group (n=25)	p-value*
Age (month); mean±SD	15.6±14.28	23.13 ±12.40	0.13
Age younger than 2 years old; n (%)	16 (65)	16 (65)	1.0
Male; n (%)	15 (60)	10 (40)	0.27
Weight (kg), mean±SD	10.0±4.54	11.2±2.91	0.39
Diagnosis category		0.70	
Pneumonia	22	20	
Bronchiolitis	2	3	
Bronchitis	1	2	
Accessory respiratory muscle use ≥2 sites; n (%)	22 (92)	22 (88)	0.36
RAS before use HFNC; median (min, max)	7 (6, 8)	7 (5, 8)	0.83
Initial flow rate of HFNC (L/minute/kg); mean±SD	1.16±0.46	1.20±0.37	0.49
Maximum flow rate of HFNC (L/minute/kg); mean±SD	1.51±0.75	1.40±0.45	0.63
RAS after use HFNC for 1 hour; median (min, max)	4 (4, 5)	4 (4, 5)	0.73
Patients failed on protocol (did not wean); n (%)	2 (8)	1 (4)	0.79

RAS=respiratory assessment score; HFNC=high flow nasal cannula; SD=standard deviation

* p-value: comparison of two independent mean with t-test or rank sum test, comparison of two independent proportions with Fisher's exact test

the weaning (RR, HR, and SpO_2) were compared between the two groups as the pre-weaning protocol group versus the post-weaning protocol group, using multivariate linear regression with control for risk factors. Comparisons with p-values of less than 0.05 were considered statistically significant.

Results

Between August 2018 and July 2019, before implementing the weaning protocol, there were 25 patients included in the pre-weaning protocol group. After implementing the protocol, between August 2019 and July 2020, 25 patients were included in the post-weaning protocol group. The post-protocol group was younger (mean age of 15.6±14.28 months compared to 23.13±12.40 months), but the number of patients younger than two years old was similar in both groups. There was no statistical difference regarding the patients' age. The main diagnosis of both groups was pneumonia, while others were bronchiolitis and bronchitis. Severity of respiratory distress, as shown by accessory muscle use and RAS before using HFNC, was the same in both groups. The initial flow rates of HFNC in the pre-protocol group and post-protocol group were 1.2 and 1.16 L/minute/kg, respectively, with no significant difference (p=0.49) between the two. With regard to the maximum flow rate of HFNC, there was no difference between the two groups as the pre-protocol versus the post-protocol values were 1.4 versus 1.5 L/minute/kg (p=0.63). The details of all baseline characteristics are shown in Table 1.

The authors performed multivariate analysis, using linear regression adjusted for age, gender, weight, RR, HR, SpO_2, and RAS before using HFNC, and found that the post-weaning protocol group reached the initial time to wean significantly faster at 22.0±10.01 hours compared to 35.4±20.60 hours (p=0.022). In addition, the post-weaning protocol group had a significantly shorter duration of weaning time at 49.5±37.0 hours compared to 84.2±62.8 hours (p=0.034). Furthermore, the duration of HFNC support in the post-protocol group was significantly shorter than the pre-protocol group at 71.53±36.7 hours compared to 119.6±78.2 hours (p=0.019). Finally, the LOS in the post-weaning group appeared to be shorter than in the pre-weaning group, but the difference was not statistically significant. Detailed data of linear regression are shown in Table 2.

The clinical parameters, which consisted of RR, HR, and SpO_2, before using HFNC, one hour after using HFNC, one hour after weaning, and four hours after weaning, were not significantly different statistically, as shown in Table 3.

Discussion

HFNC is considered a pertinent non-invasive ventilation in children with an acute lower respiratory tract infection[2-6]. In the present study setting, patient-care staff can adjust the initial flow rate to the maximum flow rate according to the patients' clinical conditions confidently, where a flow rate of at least 6 L/minute is determined as high flow and a flow rate of 2 L/kg/minute is the maximum starting flow[7,9,10,17].

Table 2. Comparison for duration of weaning, length of time using HFNC, and length of hospital stay between groups

Durations	Post-protocol (n=25) mean±SD	Pre-protocol (n=25) mean±SD	Compared duration in 2 groups* mean	95% CI*	p-value*
Initial time to wean (hour)	22.0±10.01	35.4±20.60	–19.19	–35.32 to –3.05	0.022
Duration of weaning (hours)	49.5±37.0	84.2±62.8	–52.11	–99.88 to –4.34	0.034
LOT on HFNC (hours)	71.53±36.7	119.6±78.2	–71.31	–129.69 to –12.90	0.019
LOS (days)	7.0±2.1	7.7±4.5	–1.95	–4.89 to +0.99	0.18

LOT=length of treatment; HFNC=high flow nasal cannula; LOS=length of hospital stay; SD=standard deviation; CI=confidence interval

* Multiple linear regression adjusted to age, sex, weight, RR. HR, SpO_2, RAS before use HFNC

Table 3. Comparison of clinical parameter before and after weaning

Clinical parameters	Post-weaning protocol group (n=25); mean±SD	Pre-weaning protocol group (n=25); mean±SD	p-value*
Before use HFNC			
Respiratory rate (breath/minute)	51±7	48±12	0.41
Heart rate (beat/minute)	148±15	152±16	0.30
Oxygen saturation (%)	94.1±2.8	96.2±2.7	0.06
After use HFNC for 1 hour			
Respiratory rate (breath/minute)	44±9	45±8	0.93
Heart rate (beat/minute)	135±10	143±13	0.07
Oxygen saturation (%)	98.6±1.8	98.9±1.38	0.57
After weaning HFNC for 1 hour			
Respiratory rate (breath/minute)	43±8	41±7	0.49
Heart rate (beat/minute)	127±16	132±15	0.33
Oxygen saturation (%)	97.8±1.2	98.2±1.8	0.62
After weaning HFNC for 4 hours			
Respiratory rate (breath/minute)	42±8	41±7	0.49
Heart rate (beat/minute)	126±15	130±16	0.34
Oxygen saturation (%)	98.2±2.1	98.4±1.8	0.71

HFNC=high flow nasal cannula; SD=standard deviation

* p-value: comparison of two independent mean with t-test or rank sum test

On the contrary, their lack of knowledge regarding how to wean the flow rate made them uncomfortable with rapid weaning of HFNC flow. Therefore, the children with lower respiratory tract infection who used HFNC had prolonged length of treatment.

HFNC requires experienced staff and close monitoring in a setting equipped for rapid implementation of invasive ventilatory support. Decreased length of HFNC usage can reduce staff workload, occupancy rates in PICUs or intermediate care wards, and admission cost per patient, and might decrease the length of treatment and hospital stay. The HFNC weaning protocol has to be explicit and allow all staff to understand it. The weaning protocol in the present study was modified from the "HFNC Holiday Protocol" to be suitable for the staff to practice. This routine-to-research (R2R) study was designed to confirm that customized weaning guidelines facilitate HFNC weaning to the low-flow cannula and safe transfer of patients to the general ward.

The clinical parameters associated with treatment failure of HFNC are being a patient younger than two years old, being a patient who has chronic underlying disease, having no decrease in HR and RR within four hours of using HFNC, and having high $PaCO_2$ and low pH in blood gas[11,18-20]. In the present study, the patients' pre-intervention factors were considered confounding factors, such as age, diagnosis, weight, and disease severity. The number of patients younger than two years old was balanced between the two groups, but the mean age in the post-weaning protocol group was less than in the pre-weaning protocol group. However, this difference was not statistically significant. The severity of patients' clinical conditions was assessed from RR, HR, SpO_2, accessory respiratory muscle use, and RAS score. There were no differences in any of the clinical parameters between groups.

Most of the patients in the present study were diagnosed with pneumonia and had a highly successful weaning rate of 90% in the post-weaning protocol group and 95% in the pre-weaning protocol group. In the same way, previous HFNC weaning protocol studies have reported success rates of weaning between 83% and 90%[1,3]. Other reports had shown that a high weaning failure rate of 20% to 30% was due to the children having underlying disease that was a risk for progressive respiratory infection[4,5,11]. Because of the inclusion of non-randomized participants in the present study, the authors excluded the patients with risk factors for severe pneumonia by harmonizing baseline characteristics between the pre- and post-weaning protocol groups. Hence, the success rate in the present study might not be representative of all children with lower respiratory tract infection who used HFNC.

The post-weaning protocol group could initially wean 13.4 hours earlier than the pre-weaning protocol group (95% CI –35.3 to –3.05; p=0.022). The duration of weaning in the post-weaning protocol group was 49.5 hours, which was 34.7 hours less than the pre-weaning protocol group (95% CI –99.8 to –4.34; p=0.034). The total time spent using HFNC decreased significantly in the post-weaning protocol group. The application of the weaning protocol could decrease the length of HFNC usage by 48 hours (95% CI –129.69 to –12.90; p=0.019). The prior reports on length of HFNC treatment and length of stay, which were based on HFNC use in bronchiolitis[18,19], showed the length of HFNC treatment for bronchiolitis ranged from 43 to 72 hours and the length of stay ranged from one to six days[21-23]. The length of HFNC use and length of stay reported in those reports were shorter than those of the present study. Nevertheless, they were reasonable because most of the children in the present study were diagnosed with pneumonia.

The LOS in the post-weaning protocol group appeared to be shorter than in the pre-weaning protocol group, but this difference was not statistically significant at seven days versus eight days (95% CI –4.89 to 1; p=0.18). The insignificant difference in the length of stay might be due to the small number of participants. However, the decreased length of stay in the post-weaning protocol group corresponds to the results of previous studies by Wiser et al.[3] and Charvat et al.[24], which revealed that the use of a standard initial HFNC and weaning protocol reduced the length of stay by one to two days. However, prior studies had illustrated that HFNC use might increase the length of treatment and length of stay[25]. Therefore, it is difficult to compare the length of treatment and stay between studies because of the broad spectrum of illness severity, including patient populations and definitions of HFNC. Regarding the clinical conditions of patients at one and four hours after HFNC weaning, there was no difference in conditions between the pre- and post-weaning protocol groups. These data suggest that rapid weaning in stable patients is safe and maximizes the benefit of HFNC due to the reach of the inspiratory demands of patients.

To the authors' knowledge, the present study is the first HFNC weaning protocol study in Thailand. The limitations of the present study were the lack of randomization in therapeutic trials and the small number of participants. However, the known confounding factors were balanced between the two groups and were adjusted by using multivariate regression. There was sufficient evidence to evaluate the effect of intervention.

Conclusion

The HFNC weaning protocol promotes rapid and safe weaning from HFNC. The duration of weaning decreased from 84.2 hours to 49.5 hours after the implementation of the protocol (p=0.03). The length of time using HFNC was decreased to two days in the post-weaning protocol group at 71.53±36.7 hours versus 119.6±78.2 hours (p=0.019) without any difference in weaning failure rate and clinical parameters during weaning.

What is already known on this topic?

HFNC is used as first-line non-invasive ventilation in children with respiratory distress.

What this study adds?

The HFNC weaning protocol created to be suitable for the context can improve active weaning of HFNC and reduce duration of weaning and the length of time using HFNC.

Conflicts of interest

The authors declare no conflict of interest.

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