Impact of High-Flow Nasal Cannula Use on Neonatal Respiratory Support Patterns and Length of Stay

Suma B Hoffman MD, Natalie Terrell NNP, Colleen Hughes Driscoll MD, and Natalie L Davis MD MMSc

BACKGROUND: Heated humidified high-flow nasal cannula (HFNC) is thought to be comparable with nasal CPAP. The effect of multimodality mid-level respiratory support use in the neonatal ICU is unknown. The objective of this work was to evaluate the effect of introducing HFNC on length of respiratory support and stay. METHODS: A chart review was conducted on subjects at 24–32 weeks gestation requiring mid-level support (HFNC/nasal CPAP) 1 y before and after HFNC implementation. The 2 groups were compared for clinical and demographic data using t test or chi-square analysis. Further, multivariate linear and logistic regression was done to determine significant risk factors for outcomes controlling for covariates. RESULTS: Eighty subjects were eligible in the pre-HFNC group, and 83 were eligible in the post-HFNC group. Subjects were similar in their baseline characteristics. In clinical outcomes, the post-HFNC group had higher rates of retinopathy of prematurity ($P = .02$) and a trend toward higher bronchopulmonary dysplasia rates ($P = .063$). The post-HFNC subjects had longer duration of mid-level support and were older at the time they were weaned to stable low-flow nasal cannula ($P < .05$). Although the length of respiratory support and stay and corrected gestational age at discharge were similar, those in the pre-HFNC period were more likely to be receiving full oral feeds and be discharged home versus being transferred to an intermediate care facility ($P < .05$). CONCLUSIONS: HFNC introduction was significantly associated with a longer duration of mid-level respiratory support, decrease in oral feeding at discharge, increased retinopathy of prematurity rates, and higher use of intermediate care facilities, leading us to examine our noninvasive ventilation and weaning strategies. *Key words: neonate; high-flow nasal cannula; nasal CPAP; respiratory distress syndrome.* [Respir Care 0;0(0):1–•. © 0 Daedalus Enterprises]

Introduction

Premature infants, especially those born at very low birthweight (<1.5 kg) and extremely low birthweight (<1

kg), often have long lengths of stay in the neonatal ICU, presenting a heavy health-care resource burden.[1] In this patient population, bronchopulmonary dysplasia (BPD) is a major cause of morbidity and mortality and contributes to the long stay in the neonatal ICU.[2] It has been shown that the use of nasal CPAP reduces the length of oxygen dependence and hospital stay.[3-6]

However, nasal CPAP is not without drawbacks. This modality is nursing-intensive, can cause nasal breakdown, and can be poorly tolerated by patients.[7,8] Due to these

Correspondence: Suma B Hoffman MD, Department of Pediatrics, University of Maryland, 110 South Paca Street, 8-S-163, Baltimore MD 21201. E-mail: shoffman@peds.umaryland.edu.

disadvantages, the use of heated humidified high-flow nasal cannula (HFNC) is increasing across the world as a noninvasive respiratory support alternative in neonates.[9,10] This modality differs from nasal CPAP in that it is a flow-based support versus a pressure-based support. The heated and humidified flow allows gas to be delivered up to 8 L/min in the neonate, promoting elimination of dead space and improvement in lung compliance.[11,12] Benefits include ease of use, reduction in nasal trauma, lower pain scores, and improved nursing care and infant-parent bonding.[13-15]

Several studies have shown HFNC to be a safe modality of providing respiratory support in premature neonates comparable with that of nasal CPAP.[12,16-21] Extubation failure rates and work of breathing have been shown to be similar between the 2 modes of ventilation, even in the extremely premature.[12,18,21,22] Concerns continue to exist regarding the safety and efficacy of this modality, with the major criticism of the modality being the unpredictable generation of pulmonary distending pressures.[11] However, current studies have not shown an increase in adverse outcomes with the use of HFNC over nasal CPAP.[12,16-21]

The effect of the availability of multiple modes of noninvasive ventilator support in a single institution is currently unknown. Even with the implementation of weaning protocols, there is the potential for multimodality noninvasive respiratory support availability to have a profound effect on the respiratory support patterns of the premature infant. We aim to evaluate whether hospital stay and exposure to respiratory support was affected by the introduction of HFNC in addition to our existing respiratory support modalities.

Methods

Study Design

A retrospective chart review was conducted in a level 4 tertiary care neonatal ICU on subjects at 24–32 weeks' gestation requiring mid-level support, defined as noninvasive ventilatory support greater than low-flow nasal cannula during 2 periods surrounding HFNC implementation. This study was approved by the University of Maryland School of Medicine institutional review board. HFNC (Vapotherm, Vapotherm, Exeter, New Hampshire), was implemented in the neonatal ICU at the University of Maryland Medical Center in May of 2012. Before the introduction of HFNC, SiPAP (Carefusion, San Diego, California) and nasal CPAP (Carefusion, San Diego, California) were the modes of mid-level support available. The pre-HFNC period was from April 2011 to April 2012; the post-HFNC period was from August 2012 to August 2013. This allowed 3 months for implementation of HFNC. For each period, demographic and clinical data were collected. The primary outcomes of the study were hospital stay and du-

QUICK LOOK

Current knowledge

High-flow nasal cannula (HFNC) is a noninvasive respiratory support mode that is being increasingly used in neonates. Although the literature has not shown an increase in adverse outcomes, there continue to be concerns about the safety and efficacy of this modality.

What this paper contributes to our knowledge

This study evaluates the effect of HFNC introduction on respiratory support and disposition patterns. Our results, showing longer duration of respiratory support, decreased oral feeding, and decreased discharge to home after HFNC implementation, underline the need to closely examine new respiratory support modalities.

ration of respiratory support. Secondary outcomes included BPD, defined as oxygen or positive pressure requirement at 36 weeks, gestation, home oxygen requirement, feeding pattern on discharge, and final disposition. Oxygen reduction tests were not used to establish the definition of BPD. In addition, we also evaluated outcomes of intraventricular hemorrhage, retinopathy of prematurity, patent ductus arteriosus, and necrotizing enterocolitis.

Inclusion and Exclusion Criteria

Infants were eligible for inclusion if they met the following criteria: (1) gestational age of 24 (0 of 7) to 32 (6 of 7) weeks and (2) required mid-level respiratory support, defined as use of HFNC, CPAP, or SiPAP. Patients were excluded for the following criteria: (1) death, (2) major congenital malformations, (3) age >2 weeks on admission, or (4) never weaned below mid-level respiratory support.

Protocol Implementation

Before HFNC implementation, education and protocol implementation were completed. Initiation, weaning, and failure guidelines were established. In the University of Maryland Medical Center neonatal ICU, HFNC was intended for use as an alternative to nasal CPAP for mild to moderate respiratory distress syndrome of any gestational age. Our institution used the flow cartridge with flow range of 2–6 L/min, with flow level being initiated at the discretion of the provider. Subjects were weaned at the discretion of the provider; however, general guidelines were to wean by 1 L/min every 12 h if F_{IO_2} requirement was ≤0.3 with improved respiratory acidosis and work of
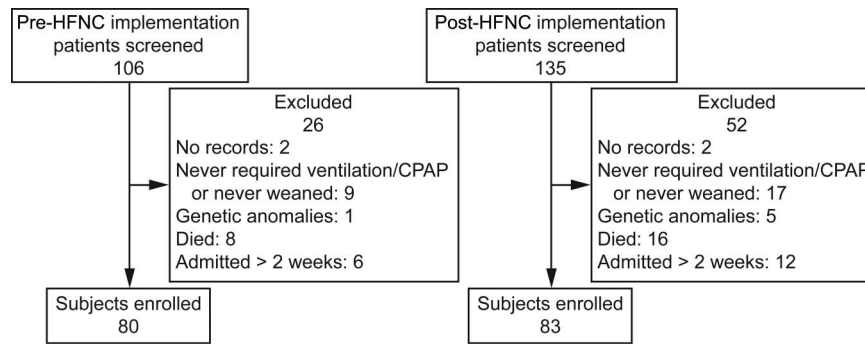
Fig. 1. Flow chart.

breathing. HFNC should be discontinued once the patient is stable receiving 2 L/min. Per the guidelines, failure of HFNC should be considered for persistent apnea, $F_{IO_2} > 0.6$, continued respiratory acidosis, or increased work of breathing despite maximizing HFNC support. Subjects were allowed to orally feed if support was <3 L/min. All staff received in-service training on the device before implementation.

Statistical Analysis

All statistical analysis was performed using SAS 9.3 (SAS, Cary, North Carolina). Continuous variables are expressed as mean (SD), and categorical data are presented as n (%). Continuous data were analyzed using a t test for parametric data and Wilcoxon rank-sum test for non-parametric data. Categorical data were analyzed using chi-square or Fisher exact testing. Multivariate linear and logistic regression was done to determine significant risk factors for primary outcomes controlling for covariates. Results for logistic regression are expressed as odds ratio and 95% CI. Statistical significance was set at $P < .05$.

Results

Of the 241 patients screened, 163 subjects were eligible, 80 in the pre-HFNC period and 83 in the post-HFNC period (Fig. 1). In the post-HFNC period, 68% of subjects were treated with HFNC, and of these subjects, 95% also were treated with nasal CPAP. In the post-HFNC period, the median number of HFNC failures (the requirement of nasal CPAP or intubation and ventilation) per subject was 0 with a range of 0–5. The majority of subjects were exposed to nasal CPAP before starting HFNC, suggesting that in practice HFNC was mainly used as a weaning modality versus a nasal CPAP alternative.

Subjects were similar in their gestational age, birthweight, sex, race, 5-min Apgar score, delivery mode, and antenatal steroid use (Table 1). There were no differences in the outcome of necrotizing enterocolitis, patent ductus

Table 1. Study Period Baseline Characteristics

| Characteristics | Study Period | | P |
	Pre-HFNC (n = 80)	Post-HFNC (n = 83)	
Gestational age, mean ± SD y	28.4 ± 2.4	28.2 ± 2.1	.48
Birthweight, mean ± SD g	1,125 ± 420	1,123 ± 362	.97
Male sex (%)	32 (40)	42 (51)	.17
5-min Apgar score, median (range)	8 (1–9)	8 (1–9)	.42
Antenatal steroids, n (%)	62 (77.5)	62 (74.7)	.59

HFNC = high-flow nasal cannula

Table 2. Study Period Outcomes

| Outcomes | Study Period | | P |
	Pre-HFNC (n = 80)	Post-HFNC (n = 83)	
NEC, n (%)	6 (7.5)	2 (2.4)	.13
ROP, n (%)	20 (25)	35 (43.2)	.02
PDA, n (%)	38 (47.5)	30 (36)	.14
IVH grade 3 or 4, n (%)	9 (11.4)	6 (7.2)	.36

HFNC = high-flow nasal cannula
NEC = necrotizing enterocolitis
ROP = retinopathy of prematurity
PDA = patent ductus arteriousus
IVH = intraventricular hemorrhage

arteriosus, culture-confirmed sepsis, and grade 3 and 4 intraventricular hemorrhage between the 2 groups (Table 2). However, in comparison with the pre-HFNC group, the post-HFNC group had higher rates of retinopathy of prematurity (25% vs 43.2%, respectively, $P = .02$) (see Table 2). No difference was noted in the need for laser therapy between groups.

As compared with the pre-HFNC group, the duration of mid-level support was significantly longer in the post-HFNC group (15 ± 15 d vs 24 ± 22 d, respectively, $P = .004$). The post-HFNC group was also older at the

Table 3. Respiratory Characteristics per Study Period

| Characteristics | Study Period | | P |
	Pre-HFNC (n = 80)	Post-HFNC (n = 83)	
BPD, n (%)	28 (35)	41 (49.4)	.063
Ventilator days, mean ± SD d	8.3 ± 14.5	9.5 ± 16.8	.62
Mid-level support days, mean ± SD d	15 ± 15	24 ± 22	.004
Age reaching LFNC, mean ± SD d	33 ± 26	52 ± 41	.005

HFNC = high-flow nasal cannula
BPD = bronchopulmonary dysplasia
LFNC = low-flow nasal cannula

Table 4. Disposition per Study Period

| Dispositions | Study Period | | P |
	Pre-HFNC (n = 80)	Post-HFNC (n = 83)	
CGA at discharge, mean ± SD wks	37 ± 3.6	37.3 ± 4.9	.69
LOS, mean ± SD d	60 ± 33	63 ± 38	.53
Per oral feeding on discharge, n (%)	58 (72.5)	35 (42.2)	<.001
Discharge to home, n (%)	54 (67.5)	36 (43.4)	.002
Discharge on oxygen, n (%)	21 (26.3)	37 (44.6)	.02

HFNC = high-flow nasal cannula
CGA = corrected gestational age
LOS = length of stay

time of reaching a stable low-flow nasal cannula (33 ± 26 d vs 52 ± 41 d, pre- vs post-HFNC, P = .005). For those who were able to wean to room air before discharge, there was no difference between the 2 periods in the day of life during which they reached stable room air. There was no difference in ventilator days or failed extubation attempts between the 2 groups. Although the difference in BPD did not reach significance, there was a trend toward higher BPD rates in the post-HFNC group (35% in the pre-HFNC group vs 49.4% in the post-HFNC group, P = .063) (Table 3).

The length of respiratory support and stay and corrected gestational age at the time of discharge were similar between the 2 groups (Table 4). However, those in the pre-HFNC period were more likely to be receiving full oral feeds at discharge (72.5% vs 42.2%, P < .001). The pre-HFNC group was less likely to be discharged receiving oxygen (26.3% vs 44.6%, P = .02). In the pre-HFNC period, 60.8% of subjects receiving oxygen at discharge were orally feeding versus only 20% in the post-HFNC group (P = .001). The pre-HFNC group was also much more likely to be discharged home versus transferred to an intermediate care facility (67.5% vs 43.4%, P = .002) (see Table 4).

Adjusting for baseline demographic and clinical factors (birthweight, gestational age, sex, antenatal steroid use, 5-min Apgar score, patent ductus arteriosus, retinopathy of prematurity, necrotizing enterocolitis, ventilator days, and BPD status), study period remained a significant predictor of the length of time receiving mid-level respiratory support using multiple linear regression, with the post-HFNC period being associated with a 5.85-d increase in mid-level support (95% CI 1.3–10.4 d) ($r^2 = 0.55$, P = .01). Utilizing multiple logistic regression, study period also remained a significant predictor of oral feeding on discharge when controlling for these baseline demographic and clinical factors in addition to time receiving mid-level support (odds ratio 0.22, 95% CI 0.097–0.508) (P < .001). When controlling for these baseline demographic and clinical factors as well as time receiving mid-level support, the only significant factor found for discharge to home versus to an intermediate care facility was oral feeding (odds ratio <0.001, 95% CI <0.001–0.019) (P < .001).

When specifically evaluating the post-HFNC period, 67.5% were treated with HFNC. For subjects exposed to HFNC, the length of respiratory support and stay was significantly longer, 71.8 (42.2) versus 47.2 (19.8) days (P < .001). There was also a trend toward decreased oral feeding on discharge for those subjects treated with multimodality support (35.9% vs 55.2%, P = .09).

Discussion

In this retrospective study of infants <33 weeks' gestation requiring mid-level respiratory support, we evaluated respiratory patterns and patient outcomes before and after the introduction of HFNC. In the post-HFNC period, we saw a significant increase in time spent receiving mid-level respiratory support. In the post-HFNC period, those subjects who required low-flow nasal cannula were significantly older upon weaning to this modality. There was no difference in the age to room air between the 2 groups. In addition, we noted a trend in the post-HFNC period toward higher BPD rates, although this did not reach statistical significance. Interestingly, there were no differences in the gestational age, birthweight, number of ventilator days, or mode of invasive ventilation between the 2 periods. This underscores that the difference in noninvasive support between the 2 periods is less likely to be due to a major difference the severity of lung disease and more likely to be secondary to the respiratory support mode itself.

There is evidence to support that nasal CPAP promotes lung growth in the premature developing lung. The consistent positive pressure provided by nasal CPAP works to keep the alveoli open, maintain functional residual capacity, and reduce the work of breathing by stenting the airway and diaphragm.[23,24] In contrast, HFNC is a modality

that works via washout of the nasopharyngeal dead space. Unlike nasal CPAP, the HFNC prongs are designed not to occlude the nares, avoiding the creation of a seal for generating positive pressure. However, there have been several studies demonstrating that flows as low as 2 L/min generate positive pressure as high as 6 cm H_2O.[25-28] To date, studies are inconsistent and show high variation in the pressures measured with HFNC.[17,25-28] This difference in the mechanism of the modality may be a plausible explanation for the increased duration of respiratory support in this population. A randomized controlled trial by Abdel-Hady et al[29] showed that weaning subjects from nasal CPAP to nasal cannula was associated with an increased oxygen exposure and duration of respiratory support. This was echoed in a study done by Sasi et al,[30] who also noted increased noninvasive respiratory times after initiation of HFNC. They felt that the inconsistent pressure generation could lead to progressive atelectasis, contributing to a prolonged duration receiving respiratory support. It may be that the consistent continuous positive pressure provided by modes such as nasal CPAP is more beneficial to premature lung development than the washout provided by HFNC.

Although we allowed a 3-month time frame for provider training and implementation, another explanation for prolonged noninvasive respiratory support in the post-HFNC period may be lack of provider comfort with the new modality and the availability of multiple modalities. This might lead to cycling through all available modalities and slower weaning. Although new technology has the potential to improve patient care, it is not without risks and requires careful consideration and implementation.[31,32] Sant'Anna and Keszler[33] advocate for a comprehensive respiratory support protocol to ensure optimal respiratory outcomes. They note that poor compliance after implementation of protocols is often due to lack of awareness or familiarity with the protocol. Although all of the providers in our institution received in-service training on both the device and the protocol, there may have continued to be some discomfort with the device that could lead to slow weaning. The time between training and actual use may have ranged beyond the 3-month period, depending on the provider's clinical schedule; this may have added to the lack of familiarity with the device. In addition, the ease of use of the device and increased patient tolerance may lead to slower weaning by the provider.

Although the increased respiratory support duration did not increase neonatal ICU stay, it may have contributed to a delay in discharge to home. Despite having a similar corrected gestational age at discharge, the post-HFNC period subjects were significantly less likely to be discharged home. In our institution, we discharge patients to a subacute facility to continue to work on oral feeding and weaning of respiratory support. An unexpected finding in this study was the delay to full oral feeding in the post-HFNC period. Although our protocol allowed for oral feeding when support reached <3 L/min, it may be that providers were hesitant to initiate oral feeds until patients were weaned to low-flow cannula. The majority of studies evaluating the use of HFNC did not include feeding pattern in their secondary outcomes. In the 2 studies we identified as examining feeding pattern differences as either a primary or secondary outcome, neither noted a difference in time to full oral feeds with the use of HFNC; however, neither study specified their feeding protocol for subjects receiving respiratory support.[34,35] These findings are counterintuitive, since the HFNC setup should promote oral feeding. There is evidence that hypercapnia and subsequent increased respiratory drive may decrease the rate of sucking and swallowing in preterm infants.[36] Although the modality itself should not directly interfere with oral feeding, the inconsistent pressure generation may lead to atelectasis and hypercapnia, which may indirectly delay feeding.

Another unexpected finding was the increased rate of retinopathy of prematurity. During the entire study time frame, we maintained the same targeted oxygen protocol. The only change during the post-HFNC period as compared with the pre-HFNC period was a change in ophthalmologists and a use of camera technology that may have led to increased diagnosis of the lower stages. This idea is supported by the fact that there was no difference in the need for laser therapy between groups. Although this 1-y pre- and post-intervention study is limited by its retrospective design and relatively small numbers, we were able to show strong trends in respiratory support use and disposition status between the 2 periods. The similarity in baseline characteristics in the 2 groups is a clear strength of the study. Also, limiting the overall study time frame to 2 y decreases confounding factors of practice variability that may affect patient outcomes.

Conclusions

The popularity of HFNC is increasing secondary to its ease of use and increased patient tolerance. However, in our institution, the introduction to HFNC was associated with significantly increased time receiving respiratory support, decreased oral feeding on discharge, and decreased rates of discharge to home. This study underlines the need to closely examine new respiratory support modalities on an ongoing basis to ensure optimal respiratory outcomes.

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