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High Flow Nasal Cannula Use Is Associated with Increased Morbidity and Length of Hospitalization in Extremely Low Birth Weight Infants

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Abstract

Objective—To determine differences in the incidence of bronchopulmonary dysplasia (BPD) or death in extremely low birth weight infants managed on high flow nasal cannula (HFNC) vs continuous positive airway pressure (CPAP).

Study design—This is retrospective data analysis from the Alere Neonatal Database for infants born between January 2008 and July 2013, weighing ≥ 1000 g at birth, and received HFNC or CPAP. Baseline demographics, clinical characteristics, and neonatal outcomes were compared between the infants who received CPAP and HFNC, or HFNC $\pm$ CPAP. Multivariable regression analysis was performed to control for the variables that differ in bivariate analysis.

Results—A total of 2487 infants met the inclusion criteria (941 CPAP group, 333 HFNC group, and 1546 HFNC $\pm$ CPAP group). The primary outcome of BPD or death was significantly higher in the HFNC group (56.8%) compared with the CPAP group (50.4%, $P < .05$). Similarly, adjusted odds of developing BPD or death was greater in the HFNC $\pm$ CPAP group compared with the CPAP group (OR 1.085, 95% CI 1.035–1.137, $P = .001$). The number of ventilator days, postnatal steroid use, days to room air, days to initiate or reach full oral feeds, and length of hospitalization were significantly higher in the HFNC and HFNC $\pm$ CPAP groups compared with the CPAP group.

Conclusions—In this retrospective study, use of HFNC in extremely low birth weight infants is associated with a higher risk of death or BPD, increased respiratory morbidities, delayed oral feeding, and prolonged hospitalization. A large clinical trial is needed to evaluate long-term safety and efficacy of HFNC in preterm infants.

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The authors declare no conflicts of interest.

Despite the use of antenatal corticosteroids, surfactant replacement therapy, and gentle ventilation, bronchopulmonary dysplasia (BPD) remains a significant problem in preterm infants.¹ There are several contributing factors to the development of BPD, including infection, hyperoxia, and ventilator-induced lung injury. In an effort to reduce injury from mechanical ventilation, noninvasive modes of respiratory support are increasingly being used.²

Continuous positive airway pressure (CPAP) is a widely used mode of noninvasive respiratory support in premature newborns. CPAP reduces extubation failure and can be used to treat apnea of prematurity.³ The use of CPAP may reduce BPD as it minimizes duration of mechanical ventilation.^{4,5} CPAP can be difficult to apply to the nares and may cause agitation, trauma to the nasal septum, and distortion of the nares.^{6–8} Alternatively, high flow nasal cannula (HFNC) is a mode of noninvasive respiratory support that is easily applied, reduces nasal trauma, and well tolerated by neonates.^{6,9} HFNC is used as an alternative to CPAP to treat respiratory distress syndrome, to facilitate extubation, and to treat apnea of prematurity.^{6,10} Using higher flow rates may result in positive end-expiratory pressure; however, pressure generated by HFNC is not measured or regulated by the circuit.^{6,10} End-distending pressure from HFNC cannot be predicted and unregulated distending pressure generated by HFNC may be injurious to the lungs.¹¹

Recent studies comparing HFNC and CPAP in preterm infants focused on short-term respiratory outcomes or were performed in larger preterm infants.^{12–15} Our objective was to evaluate whether the use of HFNC compared with CPAP reduces the risk of BPD or death in extremely low birth weight (ELBW) infants (birth weight [BW] < 1000 g). In addition, we evaluated the impact of HFNC use on oral feeding, respiratory support, and other neonatal morbidities associated with prematurity.

Methods

This study is a retrospective data analysis from the Alere Neonatal Database for infants born between January 2008 and July 2013, weighing < 1000 g at birth, and received HFNC or CPAP. Alere provides neonatal care management services for multiple private, government, and self-insured employer health plans. Alere's neonatal database is comprised of standardized clinical, sociodemographic, and cost-related information pertaining to infants admitted to the neonatal intensive care unit (NICU) in over 1000 hospitals nationwide. All infants included in the study were admitted to a level II or level III NICU, in both community and academic settings. Daily clinical, sociodemographic, and cost-related information was abstracted concurrent with each hospitalization 3–4 times per week by experienced neonatal nurses. Not all eligible infants in the study sites are enrolled because only infants in health plans managed by Alere are included in the database. The infants were cared for in 466 level II or higher academic and community-hospital based NICUs. The infants were divided into the CPAP, HFNC, and the HFNC $\pm$ CPAP groups. The infants in the CPAP group received CPAP and not HFNC during their hospitalization. The infants in the HFNC group received HFNC and not CPAP during their hospitalization. The infants in the HFNC $\pm$ CPAP group received HFNC with or without CPAP during their hospitalization. The HFNC $\pm$ CPAP group included infants who received HFNC without CPAP (same

infants who are in HFNC group), and infants who received both HFNC and CPAP (HFNC plus CPAP). The Institutional Review Board at Thomas Jefferson University Hospital approved this study.

The primary outcome was BPD or death. BPD was defined as any supplemental oxygen requirement at 36 weeks post-menstrual age (PMA). No physiological test was performed to diagnose BPD. The criteria were similar for all institutions. BPD was defined at 36 weeks PMA and death at any time during the NICU admission. The infants who were not on supplemental oxygen at 36 weeks PMA and died at 37 weeks were classified as "Death."

Prespecified secondary outcomes were ventilator days, postnatal steroid use, days to room air, days to initiate oral (PO) feeds, days to reach full PO feeds, length of hospitalization, patent ductus arteriosus requiring medical therapy, modified Bell stage 2 or higher necrotizing enterocolitis, severe intraventricular hemorrhage defined as grade 3 or 4, and retinopathy of prematurity requiring laser therapy. Baseline demographics, clinical characteristics, and neonatal outcomes were compared between the infants who received CPAP and HFNC or HFNC $\pm$ CPAP.

Statistical Analyses

Statistical analysis was performed using the Sigma plot v 13 (Systat Software, Inc, Point Richmond, California) and SPSS v 22 (IBM Corporation, Armonk, New York). The groups were compared by Student *t* tests, Mann-Whitney U tests, or χ^2 tests as appropriate. The clinical and demographic characteristics that were significantly different between the CPAP and HFNC $\pm$ CPAP groups in bivariate analyses were adjusted in multivariable regression models. Linear and logistic regression models were used and adjusted for gestational age (GA), BW, centers, 5-minute Apgar score, ventilated on day 1, ventilated at any time, and surfactant. The difference was considered significant for $P < .05$.

Results

The total number of infants born with BW $\geq$ 1000 g during the study period was 3026. We excluded 539 (17.8%) infants as they did not receive CPAP or HFNC (334 infants died and never extubated to CPAP or HFNC, 68 infants remained intubated at discharge, 137 infants did not receive CPAP or HFNC as respiratory support during the NICU stay). A total of 2487 infants met the inclusion criteria; 941 infants received CPAP, 333 infants received HFNC, and 1546 infants received HFNC with or without CPAP (HFNC $\pm$ CPAP). The HFNC $\pm$ CPAP group included infants who received HFNC with CPAP (1213 infants) and HFNC without CPAP (333 infants). The order in which the infants in this group received HFNC or CPAP is not known. In addition, the CPAP pressure and the HFNC liter flow were not known for the infants.

The clinical and demographic characteristics of the study population are summarized in Table I. There was no significant difference in GA, BW, and other baseline characteristics between the CPAP and HFNC groups. The HFNC $\pm$ CPAP group differed from the CPAP group in GA, BW, 5-minute Apgar score, and the number of infants ventilated on day 1, ventilated at any time and received surfactant.

Primary Outcome

The primary outcome of BPD or death was significantly higher in the HFNC group compared with the CPAP group (Table II). Similarly, adjusted odds of developing BPD or death was greater in the HFNC $\pm$ CPAP group compared with the CPAP group (OR 1.085, 95% CI 1.035–1.137, $P = .001$).

Respiratory Outcomes

The number of infants who developed BPD was significantly higher in the HFNC group compared with the CPAP group (Table II). The days on mechanical ventilation, use of postnatal steroids, and days on oxygen was also higher with the use of HFNC. Similarly, the adjusted odds of developing BPD was greater in the HFNC $\pm$ CPAP group compared with the CPAP group (OR 1.168, 95% CI 1.118–1.220, $P < .001$). In addition, more infants in the HFNC $\pm$ CPAP group required multiple ventilator courses, received postnatal steroids, and had longer days on a ventilator and oxygen.

Feeding Outcomes and Length of Hospitalization

Time to initiate PO feeds, time to achieve full PO feeds, and length of hospitalization were significantly longer in infants in the HFNC group compared with the CPAP group (Table III). Similarly, after adjusting for confounding variables, infants in the HFNC $\pm$ CPAP group took longer to initiate PO feeds, achieve full PO feeds, and were hospitalized longer when compared with the CPAP group.

Other Neonatal Outcomes

The other neonatal morbidities associated with prematurity (severe intraventricular hemorrhage, patent ductus arteriosus, necrotizing enterocolitis, and retinopathy of prematurity requiring laser therapy) did not differ in infants who received HFNC and CPAP (Table II). After adjusting for confounding variables, the differences in neonatal morbidities associated with prematurity were also similar in the CPAP and HFNC $\pm$ CPAP groups (Tables II and IV).

High Volume vs Low Volume Centers

The data analysis included infants from 466 hospitals. The number of infants per hospital ranged between 1 and 105. Three hundred seventy-eight low-volume centers (<10 infants from the study site) contributed 976 infants (39%); 88 high-volume centers (10 or more infants from the study site) contributed remaining 1511 infants (61%). Baseline demographics and neonatal outcomes were compared in low volume and high volume centers and presented in Tables V and VI (available at www.jpeds.com). Similar differences in outcomes were found in low volume as well as high volume centers except for BPD or death. In low volume centers, the rate of BPD or death was not statistically different between the CPAP and HFNC groups (there was a trend toward higher BPD or death with the use of HFNC). This is likely to be due to smaller sample size.

Discussion

Despite limited data, HFNC is commonly used in preterm infants to wean from CPAP or as an alternative to CPAP. Randomized clinical trials investigating the short-term outcomes showed similar or greater re-intubation rates with the use of HFNC compared with CPAP.^{12–15} In this first study comparing use of HFNC and CPAP in ELBW infants, we found that infants managed on HFNC were at higher risk of BPD or death. Similarly, the use of a combination of HFNC and CPAP was associated with increased risk of BPD or death in ELBW infants. In addition, infants in the study population who received HFNC or a combination of HFNC and CPAP were on oxygen for a prolonged period of time, took longer to begin and reach full oral feeds, were more likely to be treated with postnatal steroids, and had a longer length of hospitalization.

Although several factors contribute to the development of BPD in ELBW infants, ventilator-induced lung injury had a key role in its pathogenesis. The use of CPAP as a mode of noninvasive ventilation reduces the incidence of BPD or death.¹⁶ However, the use of CPAP in ELBW infants may be limited due to difficulty applying it to the nares and by the risk of nasal trauma. The use of HFNC in ELBW infants may provide an alternative mode of noninvasive respiratory support because of the ease of application, improved tolerance, and less nasal trauma.^{9,13} HFNC can reduce work of breathing, improve lung compliance, and deliver some degree of positive airway pressure.^{9,17,18} Because of the presence of a leak within the airway, there is significant variability in the distending airway pressure generated with HFNC. When HFNC was used in preterm infants with respiratory distress syndrome, presence of a 30% leak reduced the airway distending pressure to <3 cm of H₂O.¹¹ With the flow rate as high as 5 liters per minute (LPM), no pressure was generated in preterm and term infants when the mouth was open.¹⁹ Even at a flow rate of 8 LPM, the mean pharyngeal pressure generated by the 2 commonly used HFNC devices was 4.9 and 4.1 cm of H₂O.¹³ In contrast, if the infant's mouth is closed or there are dried secretions around the nares, the continuous high flow can increase the airway pressure to an undesirable level. Locke et al²⁰ demonstrated that even with a flow rate of 2 LPM, it is possible to generate airway pressures of 12 cm of H₂O. The currently available HFNC delivery systems do not measure the airway pressure, nor prevent excessive pressure delivery to the infant's airway. Unregulated distending airway pressure generated by HFNC may lead to lung injury either because of overexpansion or atelectasis and can contribute to the development of BPD. More infants in the HFNC ± CPAP group required more than 3 ventilation courses suggesting extubation failure with the use of HFNC. Manley et al¹⁴ also reported a trend toward higher rates of extubation failure with the use of HFNC (HFNC 34.2% vs CPAP 25.8%). Extubation failure leads to prolonged cumulative ventilator support. Recently, we have shown that cumulative days of ventilatory support and 4 or more ventilator courses are associated with BPD and respiratory morbidities in ELBW infants.²¹ Another possibility for prolonged respiratory support with the use of HFNC is that caregivers perceive HFNC to be “low risk” and are slower to wean or stop it. Yoder et al¹⁵ reported that infants managed on HFNC require prolonged noninvasive respiratory support. Abdel-Hady et al²² also reported that weaning from CPAP to HFNC limited to 2 LPM was associated with longer duration of

oxygen and respiratory support compared with infants who remained on CPAP until weaned directly to room air.

Several randomized controlled trials (RCTs) compared extubation failure with the use of HFNC and CPAP. Campbell et al¹² randomized 40 neonates (BW <1250 g) to HFNC or CPAP after extubation. Extubation failure, oxygen requirement, and number of episodes of apnea and bradycardia per day were higher for infants in the HFNC group. However, the flow rates used in this trial were lower (1.4–1.7 LPM) than those in current clinical use. Collins et al,¹³ in a RCT enrolling 132 ventilated preterm infants (<32 weeks gestation), found no difference in extubation failure between CPAP and HFNC groups when higher flow rates (8 LPM) were used. However, this study was underpowered to detect the difference in extubation failure. A larger clinical trial, enrolling 303 preterm ventilated infants (<32 weeks gestation), showed a trend toward higher rates of treatment failure with the use of HFNC (HFNC 34.2% vs CPAP 25.8%).¹⁴ A study by Yoder et al¹⁵ was the largest RCT (432 infants) comparing rate of intubation within 72 hours of initiating CPAP or HFNC. They found no difference in the primary outcome as well as rate of BPD, days on oxygen, and home oxygen use between the 2 groups. However, they excluded ELBW infants from the study. The study enrolled infants ranging between 28 and 42 weeks of gestation, and only 75 infants in each group were <32 weeks gestation. Moreover, the median age of noninvasive support was only 2 days for CPAP and 4 days for HFNC.¹⁵

Our data indicate that the use of HFNC in ELBW infants not only increased respiratory morbidities but also prolonged establishment of oral feeds and the length of hospitalization. There is no literature to guide weaning the rate of flow for infants on HFNC. Similarly, there are no guidelines on PO feeding infants while receiving HFNC. In addition, infants managed on HFNC require prolonged noninvasive respiratory support.¹⁵ A reason commonly cited for using HFNC in infants is that, compared with CPAP, it “frees-up” the infants face and makes it easier for them to feed. Our data do not support this belief. Caregivers perceive the use of HFNC as equivalent to CPAP and likely hesitant to PO feed. At our institution, PO feeding is not initiated unless the infant is on HFNC with liter flow of 2 or less. We speculate that initiating PO feeding is delayed in infants on HFNC as clinicians are reluctant to PO feed while an infant is requiring noninvasive respiratory support. The delay in initiating PO feeds also results in a delay in achieving full PO feeds and subsequently prolongs hospitalization.

There are 3 possibilities for increased respiratory morbidities, delayed PO feeding, and prolonged hospitalization with the use of HFNC. The difference could be due to chance. However, the strength of the association makes this unlikely. The difference in outcomes could also be due to a difference in baseline demographic and clinical characteristics between the groups. There is no significant difference in the CPAP and HFNC groups in BW, GA, 5-minute Apgar scores, and other markers of severity of illness. When comparing differences in outcomes between infants in the HFNC ± CPAP group and CPAP group, multiple regression analysis was used to adjust for the differences between the groups. It is highly likely that the adverse outcomes in infants in the HFNC and HFNC ± CPAP groups are due to the use of HFNC.

This study has several strengths. We compared the use of HFNC and CPAP in ELBW infants and to evaluate BPD or death as a primary outcome. Another important strength is the large sample size. The results from this study should be broadly generalizable as the analysis included infants from 466 NICUs across the US in both academic and community settings. We recognize some important limitations of this study. This is a retrospective study; however, trained neonatal health care professionals collected the data prospectively. The infants were not randomized to receive HFNC or CPAP. The liter flow of HFNC and the pressure of the CPAP were not in the database. The order in which infants were exposed to HFNC and CPAP in the HFNC $\pm$ CPAP group also is unknown. The rate of antenatal steroid use in our cohort is low. Not all eligible infants in the study sites are enrolled, only infants with health plans managed by Alere are included in the database. It is possible that the population served by Alere has limited prenatal care with lower use of antenatal steroids. However, there was no significant difference in the use of prenatal steroids in the 3 groups in our study population.

In conclusion, our findings suggest that ELBW infants who received HFNC during hospitalization had a greater likelihood of developing BPD or death. In addition, HFNC use in ELBW infants was associated with a delay in establishing oral feeds, increased use of postnatal steroids, longer need for oxygen, and prolonged hospitalization when compared with the use of CPAP. An adequately powered RCT is recommended to evaluate the effect of HFNC on long-term respiratory morbidity, oral feeding, and length of hospitalization in ELBW infants.

Glossary

BPD	Bronchopulmonary dysplasia
BW	Birth weight
CPAP	Continuous positive airway pressure
ELBW	Extremely low birth weight
GA	Gestational age
HFNC	High flow nasal cannula
LPM	Liters per minute
NICU	Neonatal intensive care unit
PMA	Postmenstrual age
PO	Oral
RCT	Randomized controlled trial

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Table IDemographics and baseline clinical characteristics of the study population (mean $\pm$ SD)

	CPAP (941)	HFNC (333)	HFNC $\pm$ CPAP (1546)
GA (wk)	26.7 $\pm$ 2.1	26.5 $\pm$ 1.9	26.3 $\pm$ 1.8 *
BW (g)	787 $\pm$ 145	776 $\pm$ 149	773 $\pm$ 146 *
Male sex (%)	436 (46.3)	143 (42.9)	753 (48.7)
Caucasian race (%)	318 (33.8)	114 (34.2)	553 (35.8)
Chorioamnionitis (%)	42 (4.5)	10 (3.0)	92 (5.9)
Prenatal steroids (any dose) (%)	426 (45.3)	147 (44.1)	741 (47.9)
5-min Apgar <5 (%)	127 (13.5)	53 (15.9)	290 (18.7) *
Ventilated d 1 (%)	686 (72.9)	234 (70.3)	1195 (77.3) *
Ventilated any time (%)	799 (84.9)	284 (85.3)	1387 (89.7) *
Surfactant (%)	612 (65.0)	212 (63.6)	1089 (70.4) *

* $P < .05$ CPAP vs HFNC $\pm$ CPAP.

Table II

Respiratory and other neonatal outcomes in infants who received CPAP vs HFNC and CPAP vs HFNC ± CPAP

	CPAP (941)	HFNC (333)	HFNC ± CPAP (1546)
CPAP d (median, IQR)	15 (5–28)		7 (1–19)
HFNC d (median, IQR)		14 (5–25)	13 (6–23)
HFNC ± CPAP (median, IQR)	15 (5–28)	14 (5–25)	26 (14–39) [*]
BPD or death (%)	474 (50.4)	189 (56.8) [†]	950 (61.5) [‡]
BPD (%)	397 (42.2)	174 (52.2) [†]	912 (59.0) [‡]
Multiple ventilation courses (%)	481 (51.1)	177 (53.1)	1000 (64.7) [‡]
More than 3 ventilation courses (%)	166 (17.6)	70 (21.0)	454 (29.4) [‡]
Ventilator d (median, IQR)	18 (5–42)	25 (6–52) [†]	30 (10–58) [§]
Postnatal steroids (%)	115 (12.2)	71 (21.3) [†]	387 (25.0) [‡]
D to room air (median, IQR)	62 (39–90)	76 (51–103) [†]	72 (51–96) [*]
Discharge home on oxygen (%)	201 (21.4)	70 (21.0)	432 (27.9) [¶]
Severe IVH (grade 3/4) (%)	79 (8.4)	31 (9.3)	170 (11.0) [¶]
PDA requiring medical therapy	445 (47.3)	145 (43.5)	797 (51.5) [¶]
NEC Bell's stage 2 or higher	74 (7.7)	30 (9.0)	126 (8.1)
ROP requiring laser	81 (8.6)	36 (10.8)	208 (13.4) [¶]

IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity.

Gray shading indicates that no patients were in those groups (ie, CPAP group did not have any patients that received HFNC).

^{*} $P < .001$, CPAP vs HFNC ± CPAP, after adjusting for BW, GA, centers, 5-min Apgar score, ventilated on d 1, ventilator d, and use of surfactant (multiple linear regression).

[†] $P < .05$, CPAP vs HFNC.

[‡] $P < .05$, CPAP vs HFNC ± CPAP (multiple logistic regression) OR for BPD or death when on HFNC ± CPAP 1.085 (95% CI 1.035–1.137, $P = .001$), BPD; 1.168 (95% CI 1.118–1.220, $P < .001$).

[§] $P < .05$, CPAP vs HFNC ± CPAP.

[¶] No significant difference CPAP vs HFNC ± CPAP after adjusting for BW, GA, centers, ventilated on d 1, ventilator d, 5-min Apgar score, and use of surfactant (multiple logistic regression).

Table III

Feeding outcomes and length of hospitalization (median, IQR)

	CPAP (941)	HFNC (333)	CPAP ± HFNC (1546)
D PO feeds started	51 (38–65)	56 (43–73) *	59 (46–80) †
D to full PO feeds	72 (55–90)	78 (60–98) *	84 (66–106) †
Discharge weight (g)	2500 (2140–2991)	2556 (2166–3140)	2745 (2295–3328) †
Length of hospitalization (d)	82 (64–104)	89 (69–111) *	95 (75–119) †

* $P < .001$, CPAP vs HFNC.† $P < .001$, CPAP vs HFNC ± CPAP, after adjusting for BW, GA, centers, ventilated on d 1, ventilator d, 5-min Apgar score, and use of surfactant (multiple linear regression).

Table IV

OR for neonatal outcomes in infants on HFNC $\pm$ CPAP vs CPAP (adjusted for GA, BW, centers, ventilated on day 1, ventilator days, 5-min Apgar score, and surfactant use)

	HFNC $\pm$ CPAP vs CPAP	
	OR (95% CI)	<i>P</i>
BPD or death	1.085 (1.035–1.137)	.001
BPD	1.168 (1.118–1.220)	<.001
Severe IVH (grade 3 or 4)	1.077 (0.804–1.441)	.6
PDA requiring medical therapy	0.937 (0.786–1.116)	.5
NEC Bell stage 2 or higher	0.893 (0.656–1.217)	.5
ROP requiring laser	1.283 (0.961–1.712)	.1

Table V

Clinical characteristics and outcomes in infants from low volume centers (<10 infants/center) who received CPAP vs HFNC and CPAP vs HFNC ± CPAP

	CPAP (364)	HFNC (140)	HFNC ± CPAP (612)
BW (g)	800 ± 140	798 ± 148	782 ± 146
GA (wk)	26.8 ± 2.0	26.5 ± 1.9	26.3 ± 1.8 [*]
5-min Apgar <5 (%)	37 (10.2)	19 (13.6)	95 (15.5) [*]
Ventilated d 1 (%)	268 (73.6)	112 (80)	512 (83.7) [*]
Ventilated any time (%)	314 (86.3)	125 (89.3)	566 (92.5) [*]
Surfactant (%)	234 (64.3)	102 (72.9)	454 (74.2) [*]
BPD or death (%)	164 (45.1)	71 (50.7)	362 (59.2) ^{*,†}
BPD (%)	141 (38.7)	67 (47.9)	351 (57.4) ^{*,†}
Postnatal steroids (%)	40 (11.0)	26 (18.6) [‡]	144 (23.6) ^{*,‡}
D to room air (median, IQR)	60 (36–88)	74 (46–94) [‡]	82 (55–105) ^{*,‡}
D PO feeds started (median, IQR)	52 (37–67)	54 (41–67) [‡]	58 (46–72) ^{*,‡}
D to full PO feeds (median, IQR)	71 (55–88)	76 (58–96) [‡]	83 (66–104) ^{*,‡}
Length of hospitalization, d (median, IQR)	81 (63–97)	86 (62–106) [‡]	94 (74–117) ^{*,‡}

^{*}*P* < .05, CPAP vs HFNC ± CPAP.

[†]*P* < .001, CPAP vs HFNC ± CPAP after adjusting for GA, 5-min Apgar, ventilated d 1, ventilated anytime, and use of surfactant.

[‡]*P* < .05, CPAP vs HFNC.

Table VI

Clinical characteristics and outcomes in infants from high volume centers (≥ 10 infants/center) who received CPAP vs HFNC and CPAP vs HFNC $\pm$ CPAP

	CPAP (577)	HFNC (193)	HFNC $\pm$ CPAP (934)
BW (g)	779 $\pm$ 147	776 $\pm$ 149	768 $\pm$ 149
GA (wk)	26.7 $\pm$ 2.1	26.5 $\pm$ 1.9	26.3 $\pm$ 1.9 [*]
5-min Apgar <5 (%)	90 (16)	34 (17.6)	195 (20.9) [*]
Ventilated d 1 (%)	418 (72.4)	122 (63) [†]	683 (73.1)
Ventilated any time (%)	485 (84)	159 (82.4)	821 (88) [*]
Surfactant (%)	378 (65.5)	110 (57.0) [†]	635 (68)
BPD or death (%)	310 (53.7)	118 (61.1) [‡]	588 (63) ^{*,§}
BPD (%)	256 (44.4)	107 (55.0) ^{†, ‡}	561 (60.1) ^{*,§}
Postnatal steroids (%)	75 (13.0)	45 (23.3) ^{†, ‡}	243 (26.0) ^{*,§}
D to room air (median, IQR)	63 (40–94)	79 (56–106) ^{†, ‡}	82 (60–110) ^{*,§}
D PO feed started (median, IQR)	51 (37–67)	58 (44–76) ^{†, ‡}	60 (47–77) ^{*,§}
D to full PO feed (median, IQR)	72 (55–93)	79 (63–98) ^{†, ‡}	84 (67–107) ^{*,§}
Length of hospitalization, d (median, IQR)	83 (65–107)	91 (72–118) ^{†, ‡}	96 (76–122) ^{*,§}

^{*} $P < .05$, CPAP vs HFNC $\pm$ CPAP.

[†] $P < .05$, CPAP vs HFNC.

[‡] $P < .05$, CPAP vs HFNC, after adjusting for ventilated on d 1 and use of surfactant.

[§] $P < .01$, CPAP vs HFNC $\pm$ CPAP after adjusting for GA, 5-min Apgar, and ventilated anytime.