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Feeding Tolerance in Preterm Infants on Noninvasive Respiratory Support

Barbara Amendolia, DrNP, NNP, APN-BC; Kathleen Fisher, PhD, CRNP; Ruth A. Wittmann-Price, PhD, RN, CNS, CNE; Joan Rosen Bloch, PhD; Marcia Gardner, PhD, RN, CPNP, CPN; Munnaza Basit, MD; Zubair H. Aghai, MD

ABSTRACT

To evaluate differences in feeding tolerance between infants maintained on continuous positive airway pressure (CPAP) and those receiving high-flow (nasal) cannula (HFC) with or without CPAP. This is a retrospective, cross-sectional study. Two groups of very low-birth-weight infants (750-1500 g) were compared on the basis of respiratory support: (1) infants born between the January 2002 and December 2004 treated with CPAP; and (2) infants born between January 2005 and December 2006 treated with HFC with or without CPAP. The groups were compared to determine which of the two attained full feedings sooner. Successful achievement of full feedings was measured in days from birth and defined by discontinuation of hyperalimentation-supplementation and attainment of 120 mL/kg/d of enteral feedings. A total of 185 infants met inclusion criteria (103 who received CPAP exclusively and 82 who received HFC with or without CPAP). There was no statistical difference in time to full enteral feedings between the 2 groups. There was also no difference in time of initiation of oral feeding or days to full oral feedings between 2 groups. The use of HFC was not associated with changes in feeding tolerance in premature infants. Further studies are needed to investigate efficacy and potential advantages and disadvantages to the use of HFC in the very low-birth-weight infant population.

Key Words: continuous positive airway pressure, feeding intolerance, high-flow nasal cannula, very low-birth-weight

Feeding intolerance is a major problem facing the very low-birth-weight (VLBW) infant (birth weight <1500 g).[1] While technological advances have enhanced survival of infants of younger gestational ages, feeding management has not kept stride. Early nutrition has the potential to impact both short- and long-term health problems such as late-onset sepsis, necrotizing enterocolitis, rehospitalizations after neonatal intensive care unit (NICU) discharge, and early origins of adult-onset diseases.[2] Management must address problems affecting multiple organs and systems. Feeding intolerance is a major problem affecting this population. Infants with feeding intolerance require prolonged intravenous access and total parenteral nutrition, which can lead to osteopenia of prematurity, electrolyte imbalance, and total parenteral nutrition–induced cholestasis. Feeding intolerance can also delay discharge and increase healthcare costs. At the time of discharge, many VLBW infants suffer postnatal growth restriction or growth failure.[3] Decisions regarding infant feeding are often made on the basis of the respiratory stability of VLBW infants. Factors including increased work of breathing, use of and needs for various oxygen delivery devices, and increased oxygen requirements can affect the VLBW infants' ability to tolerate enteral feedings. Decisions about feeding management of these infants need to include careful consideration of respiratory instability as a significant comorbid factor.[4,5]

Traditionally, continuous positive airway pressure (CPAP) has been considered the preferred method of

Author Affiliations: Department of Pediatrics/Neonatology, Cooper University Hospital, Camden, New Jersey (Drs Amendolia, Basit, and Aghai); Drexel University College of Nursing and Health Professionals, Philadelphia, Pennsylvania (Drs Fisher and Bloch); Department of Nursing, Francis Marion University, Florence, South Carolina (Dr Wittmann-Price); and College of Nursing, Seton Hall University, South Orange, New Jersey (Dr Gardner).

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Corresponding Author: Barbara Amendolia, DrNP, NNP, APC-BC, Drexel University College of Nursing and Health Professionals, 245 N 15th St, Philadelphia, PA 19102 (bja39@drexel.edu).

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treatment for infants who no longer need intubation and ventilation.[6] High-flow (nasal) cannulas (HFCs) have recently been introduced as an alternative mode of respiratory support for this population.[7] Varying clinician preferences have directed VLBW infants to either therapy without adequate evidence to indicate which therapy is most effective. This study was designed to address this gap in the neonatal literature. We hypothesized that infants on HFC with or without CPAP would attain full feedings sooner than those treated with the more traditional CPAP alone. The purpose of this project was to evaluate differences in feeding tolerance between infants maintained on CPAP and those infants receiving HFC with or without CPAP.

RESEARCH DESIGN

A retrospective, cross-sectional design was used to complete a secondary analysis of the Neonatal Information System 3 (NIS) database. NIS 3–coded data include diagnosis, environment, respiratory support, laboratory, procedures, medications, vaccines, and nutrition (enteral and parenteral). The hospital's institutional review board approved this study.

Sample/setting

A convenience sample was drawn from an existing database at a major tertiary center on the East Coast that included all hospitalized VLBW infants on specific modes of respiratory support. Infants were divided into 2 groups. The first was a control group born between January 2002 and December 2003, which received CPAP, the traditional therapy. The second group born between January 2005 and December 2006 was the case group, which included infants receiving HFC with or without CPAP. The study hypothesis proposed that infants treated with the HFC with or without CPAP would have better feeding tolerance than those treated with CPAP alone. The time period was chosen as a reflection of the initiation of HFC therapy at the center. The study site began using HFC as a mode of respiratory support in 2004. Because 2004 was a transition year, we did not include this year in the comparison. The infants received 2 to 6 L of flow per minutes while on HFC. The aim was to investigate whether there was a difference in feeding tolerance from when HFC was used as compared with the earlier time period when only CPAP was available.

Methods

Infants weighing between 750 and 1500 g, born within the gestation range of 27 and 34 weeks who required respiratory support, were included in the study. There are different CPAP modalities used at the center (ventilator CPAP, Aladdin CPAP, and Infant Flow CPAP). All infants on any type of CPAP support were included in the study. We excluded those infants with a diagnosis of necrotizing enterocolitis, abdominal perforations secondary to infection, history of indomethacin administration, and abdominal wall defects. We also excluded infants with cardiac anomalies, congenital malformations, and grade III-IV intraventricular hemorrhage. Feeding tolerance was operationalized as time to full enteral feedings. This was measured in days, defined as the stopping of hyperalimentation and attainment of 120 mL/kg/d of enteral feedings. Baseline data were collected on gender, birth weight, and the following comorbidities and conditions: intraventricular hemorrhage, patent ductus arteriosis, sepsis, time on ventilation, mode of delivery cesarean delivery versus vaginal delivery, Apgar scores, prenatal steroids given to mother, postnatal steroids given to infants, incidence of chronic lung disease, retinopathy of prematurity, and central umbilical lines (types and duration).

Data collection

The data from the NIS-3 were used for this study. One trained data collector retrieves data from patient's bedside records on a daily basis and transcribes it onto an extensive worksheet that is coded with diagnosis (confirmed/suspected), environment, respiratory support, laboratory, procedures, medications, vaccines with dates, and nutrition (enteral and parenteral). The data collected are entered directly into the database by this same individual. Data extracted from the NIS 3 database were then coded and entered into an Excel spreadsheet. Additional data were also extracted from patient charts.

Statistics

The Sigma Stat 3.1 for Windows Statistical package was used to calculate differences between the 2 groups. The Student t test and the Mann-Whitney U test were performed for continuous data and the χ^2 or Fisher exact test for categorical data, with significance set at $P < .05$.

RESULTS

There were 185 infants who met inclusion criteria. The first group included 103 infants who were born before HFC was started, and the second group included 82 infants who received HFC with or without CPAP. There was no significant difference in the baseline demographic, clinical characteristics, and independent variable between the 2 groups (see Tables 1 and 2). The discharge weight and the weight gained per day were significantly higher in infants treated with HFC with or

Table 1. **Demographics and baseline clinical characteristics of infants in 2 groups (mean ± SD)**

	CPAP ($n = 103$)	HFC ± CPAP ($n = 82$)	*P*
Birth weight, g	1156 ± 205	1135 ± 202	.5
Gestational age, wk	28.8 ± 2.6	28.8 ± 2.0	.9
Sex (male), *n* (%)	55 (53)	45 (55)	.9
Race, black, *n* (%)	49 (48)	46 (56)	.3
Prenatal steroid, *n* (%)	82 (80)	69 (84)	.5
Vaginal delivery, *n* (%)	46 (45)	33 (40)	.6
Apgar score at 5 min, (median range)	8 (4-9)	8 (3-9)	.4
Surfactant, *n* (%)	48 (47)	38 (46)	.9
Mechanical ventilation, *n* (%)	60 (58)	46 (56)	.9
Days on mechanical ventilation	14.7 ± 17.4	11.5 ± 12.5	.5
Postnatal steroids, *n* (%)	20 (19.4)	12 (14.6)	.5

Abbreviations: CPAP, continuous positive airway pressure; HCF, high-flow (nasal) cannula.

Table 2. **The independent variables between the 2 groups (mean ± SD)**

	CPAP ($n = 103$)	HFC ± CPAP ($n = 82$)	*P*
Days on CPAP	5.3 ± 6.4	4.9 ± 6.3	.7
Days on HFC	0	20.1 ± 12.3	
Days on O_2	29.7 ± 30.5	34.5 ± 29.5	.13
Sepsis, *n* (%)	29 (28)	14 (17)	.1
Breast milk, *n* (%)	54 (52)	54 (69)	.14

Abbreviations: CPAP, continuous positive airway pressure; HCF, high-flow (nasal) cannula.

without CPAP (see Table 3). Successful achievement of full feeding was similar in 2 groups (see Table 4). There was also no significant difference in time of initiation of enteral feedings, time of initiation of oral feedings, or days to full oral feedings. A summary of descriptive statistics is listed in Tables 1 and 2 and study findings in Tables 3 and 4.

DISCUSSION

Feeding intolerance in VLBW infants continues to challenge neonatal providers. With the advent of HFC systems, clinicians now have an alternative mode of respiratory support that may help improve feeding tolerance. There is scant evidence available comparing one mode of support versus the other. A recent Cochrane review compared safety and efficacy of HFC with other forms of noninvasive respiratory support in this population. There was insufficient evidence to establish safety or efficacy of the new mode of oxygen delivery. However, the main focus was on treatment failure and rate of reintubation and not on enteral feeding tolerance as a primary or secondary outcome.[8] Optimizing neonatal nutrition involves collective functioning of both the respiratory system and the gastrointestinal system. Strategies aimed at improving enteral feeding tolerance should include each as a comorbid factor.

Although CPAP has been the preferred modality for continued support, it is not without problems. Gastric distention, air leaks, nasal trauma, and other complications have been described in the literature.[6–11] Negative aspects of nasal CPAP have been well documented. For example, nasal trauma has been reported with the

Table 3. **The dependent variables between the 2 groups (mean ± SD)**

	CPAP ($n = 103$)	HFC ± CPAP ($n = 82$)	*P*
Duration of hospitalization, d	49 ± 24	54 ± 21	.1
Weight at discharge, g	2192 ± 523	2500 ± 658	<.01
Daily weight gain, g	20.8 ± 4.2	24.8 ± 9.0	<.01

Abbreviations: CPAP, continuous positive airway pressure; HCF, high-flow (nasal) cannula.

Table 4. **Feeding outcomes in days from birth and at PMA (mean ± SD)**

	CPAP ($n = 185$)	HFC ± CPAP ($n = 82$)	*P*
Enteral feed started (age in days)	3.8 ± 2.2	3.6 ± 1.8	.8
Enteral feed started (PMA in weeks)	29.4 ± 2.2	29.3 ± 2.0	.9
Full enteral feed (age in days)	17.1 ± 13.0	16.3 ± 8.7	.3
Full enteral feed (PMA in weeks)	31.2 ± 2.2	31.6 ± 1.8	.8
PO feed started (age in days)	33.0 ± 17.8	32.0 ± 14.0	.9
PO feed started (PMA in weeks)	33.6 ± 1.6	33.3 ± 1.9	.2
Full PO feed (age in days)	44.6 ± 23.9	46.4 ± 20.3	.3
Full PO feed (PMA in weeks)	35.2 ± 2.4	35.3 ± 2.6	.8

Abbreviations: CPAP, continuous positive airway pressure; HCF, high-flow (nasal) cannula; PMA, postmenstrual age; PO, oral/orally.

use of nasal prongs.[9] Septal erosion, technical problems with positioning, maintaining an effective seal, and overhandling of infants are some other commonly reported drawbacks to CPAP use.[6,10,11] Nasal occlusion and nasal deformities have also been reported as complications of the devices.[11]

As an alternative to traditional CPAP devices, HFC systems are positioned just below the nares, using a soft nasal cannula apparatus similar to a conventional nasal cannula. The HFC systems are capable of delivering high-flow oxygen that is heated and humidified and can be blended to an appropriate concentration for desired saturation levels. There is a paucity of studies with infants on HFC, although this therapy appears to be well tolerated and safe for the neonatal population. There are still many questions in relation to best evidence-based protocols for HFC use in neonates including which infants should be considered for treatment and at what intervention point in their disease process. There are limited studies in the literature that provide guidance for placing infants on one mode of support versus another.

Advancement of enteral feeding in VLBW infants becomes the primary focus once the respiratory system has been stabilized. For this population of infants, feeding intolerance remains a significant problem. Differences in feeding practices exist on several levels. Inconsistencies in management with regard to volume and timing of the first feeding create difficulties in measuring outcomes.[12] Feeding methods and types of feedings such as breast milk or premature formula differ widely by center. Method of feedings including bolus versus continuous feedings, as well as management of the advancement of feedings, varies among clinicians and NICUs. It is not clear which strategies improve feeding tolerance and which practices do not promote optimal tolerance. A study comparing the effects of various respiratory support methods on enteral feeding tolerance in the preterm infant population would add to the limited knowledge available.

The goal of adequate nutrition is both a priority and a clinical challenge for neonatal providers.[13] Data regarding the effect of respiratory support on feeding and growth would help guide clinical practice.

The study hypothesis that infants on HFC with or without CPAP would attain full feedings sooner than those treated with the more traditional CPAP alone was not supported by the data. No significant differences were appreciated in time to full feedings between the 2 groups. Time of initiation of enteral feedings, initiation of oral feedings, and attainment of full oral feedings were also not significantly different between the 2 groups. Total days on CPAP varied widely among infants and may have affected the final results. Our study hypothesis was based on the premise that infants on CPAP would have more feeding intolerance secondary to known drawbacks of the devices such as gastric distention from high-flow, discomfort from the prongs, fatigue from overhandling, and nurses' hesitation to feed on the basis of perceived instability of the respiratory system. The analysis showed that infants in the case group spent a much longer amount of time on HFC. The higher-flow of oxygen/air that can be delivered with the system can possibly have the same complications as CPAP. However, we did not find a difference in feeding tolerance with the use of HFC.

We did find a significant difference in discharge weight and weight gain per day between the 2 groups. The infants in the case group (HFC with or without CPAP) had a significantly higher discharge weight and significantly higher weight gain per day than those in the control group. One explanation for this may be the overall improvement of feeding management over the time of the study. The infants who were treated with HFC received positive pressure from the device over a longer duration. This may have decreased work of breathing and thus contributed to improved weight gain per day and higher discharge weight than the control group.

We recognize some important limitations of this study:

1. This is a single-center retrospective study.
2. Management of preterm infants is dynamic and can vary greatly between providers and NICUs. Grouping the infants into 2 time periods may have introduced confounding variables since the overall management has changed and possibly improved over the 5-year time period and this was unavoidable.
3. Practice variation is always present in the NICU environment, and clinical judgment and individual preferences exist on many levels.
4. The number of infants having received only HFC was 3 and thus too small to analyze independently.

Despite these limitations, we conclude that the use of HFC was not associated with change in feeding tolerance in preterm infants. Our analysis adds to the limited knowledge available comparing different modes of respiratory support and their potential effects on feeding tolerance. The body of evidence surrounding HFC use is growing and suggests that it is a safe and well-tolerated therapeutic alternative to the traditional CPAP. Further studies are needed to investigate efficacy and potential advantages and disadvantages to the use of HFC in the VLBW infant population.

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