Abstract

Healthy preterm infants, 32 to younger than 34 weeks postconceptional age, (n = 81) were randomly assigned to standard care or semidemand protocols for making the transition from gavage to oral feeding. Experimental infants showed less autonomic arousal (decreased low-frequency [LF] and decreased high-frequency [HF] power) when using a pacifier before feeding compared with control infants. During oral feeding, control infants showed an increase in the sympathetic to parasympathetic balance (LF/HF) from the prefeeding period, whereas LF/HF for experimental infants did not change significantly. In the 48 hours after achieving full oral feeding, control infants had significantly more feeding bradycardia episodes than experimental infants. The semidemand protocol that included use of a pacifier before oral feeding, opportunity to feed orally up to eight times per day, and use of infant behavior to begin and end feedings resulted in the autonomic balance of the experimental infants being more stable as they learned to feed orally.

Heart Rate Variability and Feeding Bradycardia in Healthy Preterm Infants During Transition From Gavage to Oral Feeding

By Gail C. McCain, PhD, RN, FAAN, Ellen O. Fuller, PhD, and Peter S. Gartside, PhD

The immaturity of the autonomic system of preterm infants places them at risk for developing feeding bradycardia as they make the transition from gavage to oral feeding. This is particularly true for infants younger than 34 weeks postconceptional age (PCA) because the autonomic system undergoes significant maturation between 31 and 38 weeks of gestation.[1] The decrease in resting heart rates, for example, from 152 ± 2 beats per minute (bpm) at 34 to 35 weeks PCA to 135 ± 2 bpm at 40 weeks PCA, provides evidence for the continuing development of the parasympathetic role (specifically the vagal role) in regulating heart rate in this period.[2] Considering the variation in estimating PCA and the natural variation in maturation, the transition from gavage to oral feeding is a period of risk for the preterm infant because oral feeding requires an integration of sucking, swallowing, and breathing reflexes, all of which are vagally mediated.

In the clinical setting, the transition from gavage to oral feeding is a gradual process. Usual clinical practice introduces the preterm infant to oral feeding once or twice in 24 hours, followed by increasing the number of episodes of oral feeding gradually with concomitant decreases in gavage feeding until the transition is complete. On the average, for 32- to 33-week-PCA infants, the transition takes about 10 days.[3]

The early stages of the transition are often accompanied by episodes of choking, apnea, and bradycardia as preterm infants learn how to suck, swallow, and breathe in a rhythmical pattern. DiPietro et al[4] reported that preterm infants (32.5 weeks PCA) had significantly fewer feeding bradycardia episodes when they sucked on pacifiers compared with no-pacifier sucking when they were on

From the University of Miami School of Nursing and Health Studies, Miami, FL, University of Pennsylvania (Emerita) Philadelphia, PA, and Department of Biostatistics, University of Cincinnati, Cincinnati, OH.
Doctor McCain is supported by grant NINR/NIH R01 NR04083.
Address reprint requests to Gail C. McCain, PhD, RN, FAAN, University of Miami School of Nursing and Health Studies, 5801 Red Road, Coral Gables, FL 33143.

1527-3369/05/0503-0104$30.00/0
doi:10.1053/j.nainr.2005.04.005

full gavage feeding. However, the infants were not studied during oral feedings.

Heart rate variability (HRV) indices (low-frequency [LF] power, high-frequency [HF] power, and LF/HF ratios) have been used to help understand feeding bradycardia. Preterm infants (n = 12) of 34 weeks PCA with documented feeding bradycardia had higher parasympathetic activity 1 hour before oral feeding compared with controls (n = 10) without feeding bradycardia.[5] The higher baseline parasympathetic activity may have accounted for the feeding bradycardia.

We have developed a semidemand protocol to aid the transition from gavage to oral feeding.[3] The rationale for the semidemand protocol has been detailed in a previous report.[14] The protocol includes offering a pacifier for 10 minutes before starting oral feeding, providing up to eight opportunities each 24 hours for the infant to feed orally, and the use of infant behavioral state to determine readiness to feed and also to continue or terminate the feeding. The protocol was tested by comparing two groups of preterm infants who were randomized to either the semidemand feeding protocol (experimental) or the standard care protocol (control) for making the transition from gavage to oral feeding. The semidemand protocol reduced the length of time required for transition to full oral feeding from an average of 10 days for the control infants on the standard care protocol to an average of 5 days for the experimental infants.[3] The present report compares the HRV indices and episodes of feeding bradycardia occurring during use of the semidemand protocol with these indices and bradycardia occurring during use of the standard feeding protocol. Study outcomes about the time to achieve oral feeding and behavioral responses were reported previously.[3,6]

Heart Rate Variability

Definition

Heart rate, measured by counting the heart beats per minute, is a net effect of the decelerating influence of the vagal (parasympathetic) fibers and the accelerating influence of the sympathetic fibers on the inherent rhythmicity of the heart's sinoatrial node. These autonomic influences result in a continuously fluctuating heart rate and are referred to as HRV. Under resting conditions, the vagal effects, which are predominant in the vertebrate heart, vary with the respiratory cycle. During inspiration, vagal impulses reaching the heart decrease, producing an increase in heart rate; during expiration, they increase, producing a decrease in heart rate. These rate changes are too brief to be detected via a pulse or stethoscope but can be measured by creating and analyzing the beat-to-beat variation via a time series power analysis. The instrumentation and mathematics for generating such power spectra have been available commercially since the 1980s.[7,8] A time series analysis of the power spectrum generates two components of clinical interest in the neonate: an HF region at 0.15 to 2 Hz which is identified with vagal tone, and an LF region at 0.02 to 0.09 Hz which is mediated by both sympathetic and parasympathetic divisions of the autonomic system. The ratio of the LF power to HF power represents the balance between sympathetic and parasympathetic activities. Sympathetic and vagal activities are constantly interacting to regulate heart rate and rhythm. The ability to balance sympathetic and parasympathetic activities is a marker of the preterm infant's ability to maintain cardiorespiratory regulation. HRV indices provide an indirect assessment of autonomic control of heart rate. In the case of immature preterm infants, HRV indices also provide information about maturation of the autonomic nervous system. For an in-depth discussion of HRV, the reader is directed to the reports by Pumprla et al[17] and the Task Force of the European Society of Cardiology of the North American Society of Pacing Electrophysiology.[16]

Early Maturation of HRV

Maturation of the autonomic nervous system after birth corresponds with a decrease in heart rate and increases in LF and HF power. Because the sympathetic component of the autonomic nervous system predominates during fetal life and at birth, the maturational changes after birth reflect increasing development of the parasympathetic component. Term newborns younger than 24 hours of life have an average heart rate of 130 $\pm$ 8 bpm and an average LF/HF ratio of 2.69 $\pm$ 0.93.[9] In term infants, LF power increased up to 3 days of life, declined between 3 days and 1 month, and increased again between 1 and 4 months.[10] HF power increased from the first to seventh days of life, declined between 7 days and 2 months, and increased again between 2 and 6 months of life.[10] The LF/HF ratio was highest at the end of the first month of life (6.5) and lowest at 6 months of life (2.5), indicating increased sympathetic influences in the first months of life followed by decreasing sympathetic and increasing parasympathetic influences by 6 months of life.[10]

Similar to term infants, increasing PCA in preterm infants is related to a decrease in heart rate and increase in HRV.[1,11] However, maturation of the sympathetic-parasympathetic balance in preterm infants is delayed compared with term infants. In a comparison of 1-day-old term and preterm infants (34–35 weeks gestational age), the LF/HF ratios were 16.3 and 71.4, respectively, illustrating the greater sympathetic activity compared with parasympathetic activity in preterm infants.[2] By 1 to 3 months PCA, the LF/HF ratios for these preterm infants had decreased from 71.4 to 34.4 but were still higher than the value of 17.1 for the term infants of the same PCA.[2] Eiselt et al[11] found that preterm infants of 37 to 41 weeks PCA had higher heart rates (157–160 bpm) compared with term infants (133–135 bpm) at the same PCA. In infants with PCA from 28 to 41 weeks gestational ages, heart rate decreased and HRV increased in quiet sleep compared with active sleep.[1,12] These heart rate and HRV changes result from the slower more regular respirations in quiet sleep and are associated with progressive parasympathetic activity.

Long-term maturation of HRV needs further study to determine whether infants who are born prematurely will continue to have underdeveloped autonomic responses over time. The lack of a standard method for calculating the HRV indices precludes comparisons of the LF and HF indices among published studies, except for their ratios. The use of different methods for calculating HRV indices has contributed to an inability to synthesize the extant research to create normative values for HRV indices in neonates.

Methods

Subjects and Setting

Approval to conduct the study was obtained from the institutional review boards at each of the two level III nurseries which served as study sites (Children's Hospital Medical Center and Good Samaritan Hospital, both in Cincinnati, Ohio). Written informed consent was obtained from each subject's parent. Inclusion criteria were younger than 34 weeks PCA at birth and receiving total caloric requirements by enteral feeding. Exclusion criteria were infants with congenital anomalies, gastrointestinal conditions, neurological diagnoses, or intracranial hemorrhage greater than grade II. Using the minimization technique that stratified on PCA at birth, birth weight, sex, and race, subjects were randomized to the control group (standard nursery protocol) or the experimental group (semidemand protocol).[13] A total of 81 infants completed the study. Of these, 78 had sufficient data for HRV analysis.

Design

The study was a randomized experiment.

Procedures

Infants started on the study protocols when they were receiving enteral feedings of fortified human milk or commercial formula of 120 to 130 kcal/kg per day without supplemental intravenous fluids or parenteral nutrition. The control group followed the nursery's standard care protocol for learning to feed orally; the experimental group followed the semidemand protocol. Infants were studied during their transition from gavage to oral feedings (ie, human milk or formula was taken both orally and by gavage to maintain nutritional requirements) until 48 hours after they had achieved full oral feeding (ie, no need for supplemental gavage to meet caloric requirements).

When a decrease in heart rate to less than 100 bpm occurred during an oral feeding, the standard nursery care was provided. That is, the oral feeding was paused to allow the infant to recover. If spontaneous recovery did not occur, gentle stimulation by rubbing the infant's back and/or supplemental oxygen was administered. Episodes of a heart rate of less than 100 bpm for more than 20 seconds were classified as feeding bradycardia.

Standard Care Transition Protocol

The standard care nursery protocol consisted of introducing one oral feeding per day initially and then gradually increasing the number of oral feedings until the infant was on eight feedings in 24 hours. Feedings were given at 3-hour intervals with feeding time restricted to 30 minutes or less. At any oral feeding, the remaining formula was given by gavage if the infant could not ingest the total feeding volume. If apnea or bradycardia developed, the oral feeding was discontinued, and the remaining volume was given by gavage. Infants were considered to have attained full oral feeding when they were able to ingest all nutrient volumes in a 24-hour period without the need for supplemental gavage. After the infants achieved full oral feeding, infants continued on the standard care protocol for 48 hours.

Semidemand Transition Protocol

The semidemand protocol required that the infant has the opportunity to feed orally up to eight times per 24 hours beginning with the first attempt to feed orally. Details of the semidemand protocol have been published.[14] A pacifier was offered for 10 minutes every 3 hours before being offered an oral feeding. The infant's behavioral state was assessed after 10 minutes of nonnutritive sucking, and if the infant was in a state higher than sleep, an oral feeding was offered. If the infant was in a sleep state, the infant was allowed to sleep 30 minutes longer followed by a second assessment. If the infant was still in a sleep state, the infant was fed by gavage. Oral feedings were continued until the infant would not resume sucking after a pause or would fall asleep. In contrast to the standard care protocol, the infant was not encouraged to continue feeding by the nurse. As with the standard care protocol, when an infant did not ingest the full feeding volume, the remaining volume was given by gavage. Attainment of full oral feeding was determined the same as described above for the control infants. Study of the infants continued for 48 hours after achieving full oral feeding.

HRV and Bradycardia Measurements

Using data from two chest electrodes, an ANSAR-R1000 system (ANSAR, Inc, Philadelphia, PA) recorded and stored the R-R intervals and the plethysmographic record of respiratory activity of the infant for the data collection period. The system software converted digitized signals from their original time domain to a frequency domain and applied a fast Fourier transformation to the data. The transformed and averaged data were then resampled at a frequency of 4 Hz. Averages for the low frequencies between 0.04 and 0.1 Hz and for the HF 0.15 to 2.0 Hz were determined, and the variations around these averages in the instantaneous heart rates within each respiratory cycle were calculated. From these variations, power spectrum was generated. The power in the LFs of the spectrum and in the HFs or respiratory frequencies was calculated as well as the ratio of LF/HF. Only artifact-free segments were used in the data analysis. Movement and other artifacts were eliminated by comparing amplitude (height) of the R wave to be included with the amplitude for the last acceptable R wave. Waves 8% greater than the previous wave were eliminated. A fast Fourier transformation requires that a window of the frequency spectrum be defined, and the left and right margins of the window be adjusted to zero. These zeros, which are a potential source of error, were also eliminated. Other sources of error (insufficient data for analysis and poor signal) were identified from graphic printouts of the electrocardiogram and spectral data and eliminated. Overall, 50% of the data were free of artifacts. Minute heart rates were calculated by the software. Prevalence of feeding bradycardia episodes (heart rates <100 bpm for >20 seconds) was recorded by the observers.

Behavioral State Assessment

Trained observers used the Modified Anderson Behavioral Scale to assess infant behavior.[19] The instrument is designed to assess preterm infant behavioral state on a 12-point categorical scale. State 1 is "regular quiet sleep" characterized by closed eyes, regular respirations, and no movement. State 2 is "irregular sleep" characterized by closed eyes, irregular respirations, and slight movement of the face, head, or lower limbs. State 3 is "active with closed eyes" characterized by whole limb movement and sucking and swallowing during feeding. State 4 is "very active with closed eyes" characterized by total body movements. State 5 is "drowsy" characterized by opening and closing eyes and sucking and swallowing during feeding. State 6 is "alert inactive," and state 7 is "quiet awake" characterized by open eyes and no movement except for sucking and swallowing during feeding. (State 6 is differentiated from state 7 only by fixated eyes.) State 8 is "active with open eyes" characterized by whole limb movement and sucking and swallowing during feeding. State 9 is "very active with open eyes" characterized by total body movements. State 10 is "fussing," state 11 is "crying," and state 12 is hard crying with very prolonged exhalation. The modification to the scale included the addition of sucking and swallowing behaviors for states 3, 5, 6, 7, and 8. These states were similar in that the infants were awake and made no movement or calm movements. For each assessment, an infant is observed for 30 seconds, and the highest numbered state attained by the infant is assigned.

Content validity has been established by a panel of neonatal nurse clinicians/researchers and a developmental pediatrician (oral communication, G Anderson, 1995). Criterion validity has been established for the Anderson scale with the Brazelton Neonatal Behavioral State Scale (personal communication, G Anderson, 1999). Interrater reliability for scoring the Anderson scale was maintained at greater than 90% throughout the period of data collection.

Because HRV can differ between sleep and awake states, HRV data used in the analysis were those data that were collected when infants were in quiet awake behavior with none or calm movement including sucking and swallowing (ie, states 3, 5, 6, 7, 8).[15] These states comprised the predominant behavior within each measurement period (Table 1).

Data Collection

Heart rate variability data were collected during morning oral feeding for each day an infant was on a study protocol. Feedings for data collection purposes were given by the first author or one of three registered nurse research assistants, all of whom are experienced neonatal nurses. Oral feedings were given with a standard nipple (Ross, Abbott Laboratories, Columbus, OH) on a volufeed container, and infants were swaddled in a blanket with arms free and held upright at a 45° angle. Infants also were held supine at a 45° angle in the 10-minute prefeeding and postfeeding periods. Nonnutritive sucking via a preemie pacifier (Gerber Co, Inc, Gerber Products Co., Fremont, MI) was provided during the prefeeding period for the

Table 1. Percentage of Time in Quiet Awake Behavioral States Corresponding to HRV Data*

Prefeeding		Feeding		Postfeeding	
Control	**Experimental**	**Control**	**Experimental**	**Control**	**Experimental**
Transition phase					
55%	97%	89%	86%	56%	59%
Full oral feeding					
42%	86%	88%	78%	84%	69%

*Control, n = 41; experimental, n = 37.

experimental infants only. HRV data were collected continuously for 10 minutes before feeding, during feeding, and for 10 minutes after feeding. The timing of the HRV data collection was synchronized with the assessment of minute behavioral states.

Analysis

The sample characteristics between the control and experimental groups were compared with χ^2 tests for categorical data and independent *t* tests for interval level data. Arithmetic means and SDs for each of the two study groups were calculated for heart rate and bradycardia events. The HRV indices (LF, HF, and LF/HF ratio) were normalized with logarithmic transformations before data analysis. Geometric means and 95% confidence intervals were calculated for the HRV indices for each study group. Differences between the two study groups were evaluated separately for the prefeeding, feeding, and postfeeding periods. The models included the following covariables: study groups (control and experimental), PCA at birth, birth weight, sex, race, day in study (study days 1, 2, 3, etc), and caffeine therapy (yes or no). Heart rate and HRV indices were analyzed with randomized effects analysis of variance models (PROC MIXED). Feeding bradycardia events were analyzed with a generalized linear model procedure (GEN MOD). The significance level was set at $P < .05$. Statistical analyses procedures were performed on a mainframe computer using the Statistical Analysis System (SAS, SAS Institute, Cary, NC).

Limitations

Only 50% of the data were free from artifacts and were usable for analysis. With a few exceptions, studies of HRV have been done in infants under sleep conditions. The sleep state controls somewhat for motor movement and thereby maximizes the chances of obtaining artifact-free data. Because this study was conducted within a natural feeding context, infant behavior was not controlled. There were equivalent HRV data for both study groups during the feeding and postfeeding measurement periods. There were 40% fewer data from quiet awake behavior in the prefeeding measurement period for the control infants compared with experimental infants. This difference occurred as a result of the pacifier sucking intervention for the experimental infants. Pacifier sucking made the experimental infants calmer, and so they spent more time in quiet states compared with control infants. Although there were sufficient data to perform the analysis techniques, the data may be underrepresentative of HRV over the measurement periods.

Results

The control (standard care protocol) and experimental (semidemand protocol) groups were similar with

Table 2. Sample Characteristics*

	Control (n = 41)	Experimental (n = 40)
	Mean ± SD	**Mean ± SD**
PCA (weeks)		
At birth	31.4 ± 1.5	30.5 ± 1.5
At start of oral feeding	32.3 ± 0.5	32.3 ± 0.5
Birth weight (grams)	1460 ± 341	1533 ± 300
	No. (%)	No. (%)
Sex		
Male	20 (49)	23 (57.5)
Female	21 (51)	17 (42.5)
Race		
Black	8 (20)	8 (20)
White	31 (75)	28 (70)
Other	2 (5)	4 (10)
Caffeine (transition phase)**		
No	28 (68)	31 (77.5)
Yes	13 (32)	9 (22.5)

*There were no significant differences between study groups for any characteristic.

**Caffeine had been discontinued in all infants by achievement of full oral feeding.

respect to PCA at birth, birth weights, sex, and racial composition (Table 2). There were no significant differences between the study groups on any characteristic. Infants in both groups began the transition to oral feeding at an average PCA of 32 weeks. During the transition phase when the infants were learning to feed orally, 13 infants in the control group and 9 infants in the experimental group were receiving caffeine. None of the infants received caffeine by the time the transition was completed. There were no differences in heart rate, HRV indices, or bradycardia episodes that were attributable to the covariables of PCA at birth, birth weight, sex, race, day in study, or caffeine therapy.

Transition Phase

During the transition to oral feeding, the HRV indices changed in both groups as the infants moved from the prefeeding to the feeding to the postfeeding periods (Table 3). As the control infants worked at feeding, their LF power decreased by 31% and HF power by 66% with the result that their LF/HF ratio more than doubled (from 1.71 to 3.65). (All HRV indices are expressed as units of power in squared milliseconds per Hertz.) In the 10-minute postfeeding period, the control infants' LF and HF power further increased over the feeding phase values, but the disparity in the increases resulted in a decrease in the LF/HF ratio over that of the feeding period. With the gradual increases in the frequency of their oral feedings, the control infants took 10 days on the average to complete the transition from gavage to full oral feeding.[3]

The experimental infants who were using a pacifier in the prefeeding period showed an increase in both LF and HF power during oral feeding (Table 3). In the 10-minute postfeeding period, the indices of the experimental infants were similar to those obtained during the feeding period. This group required only 5 days on the average to complete their transition to full oral feeding.[3]

A comparison between the control and experimental infants during transition shows that the prefeeding values for the HRV indices differed significantly between the two groups, whereas their heart rates were similar (Table 3). The use of the pacifier by the experimental infants had the effect of lowering both the LF power (5.39) and HF power

Table 3. HRV Indices, Heart Rates, and Bradycardia Episodes During the Transition to Oral Feeding (n = 76)

	10-Minute prefeeding*	During oral feeding	10-Minute postfeeding
Control infants (n = 41)			
HRV indices	**M (LCL–UCL)**	**M (LCL–UCL)**	**M (LCL–UCL)**
LF	9.82 (8.71–11.07)	6.76 (5.97–7.66)**	9.56 (8.37–10.92)**
HF	5.72 (4.71–6.94)	1.90 (1.59–2.26)**	4.38 (3.56–5.39)**
LF/HF	1.71 (1.59–1.84)	3.65 (3.41–3.91)**	2.19 (2.02–2.37)**
	M ± SD	**M ± SD**	**M ± SD**
Heart rate	147 ± 3	152 ± 3	150 ± 4
Bradycardia	–	6 ± 5	–
Experimental infants (n = 37)			
HRV indices	**M (LCL–UCL)**	**M (LCL–UCL)**	**M (LCL–UCL)**
LF	5.39 (4.57–6.35)	8.66 (7.43–10.08)**	9.44 (7.92–11.26)
HF	1.76 (1.33–2.34)	3.14 (2.47–3.99)**	4.29 (3.22–5.72)
LF/HF	3.15 (2.80–3.54)	2.89 (2.62–3.20)	2.25 (2.00–2.54)
	M ± SD	**M ± SD**	**M ± SD**
Heart rate	149 ± 3	154 ± 2	151 ± 3
Bradycardia	–	4 ± 4	–

HRV indices are expressed as squared milliseconds per Hertz and heart rates as bpm. M indicates geometric means for HRV indices (LF, HF, and LF/HF ratio), and arithmetic means for heart rates and bradycardia episodes; LCL–UCL, lower to upper confidence limit.

*LF, HF, and LF/HF are significantly different during the 10-minute prefeeding period ($P < .001$) between control and experimental groups.

**Indicates significant within-group differences for a 10-minute prefeeding to feeding period or a feeding to postfeeding period.

(1.76) compared with the control infants (9.82 and 5.72, respectively). The disparity in the LF and HF generated a significantly higher LF/RF ratio in the experimental group compared with the control group (3.15 vs 1.71). During oral feeding, the experimental group showed almost twice the HF power (3.14) of the controls (1.90) and, consequently, a significantly lower LF/HF ratio (2.89 vs 3.65). During the 10 minutes of the postfeeding period, the HRV indices of both groups were similar. Although neither group experienced bradycardia in either the prefeeding or postfeeding periods, the prevalence of feeding bradycardia episodes was similar in both groups during feeding (control mean, 6 ± 5; experimental mean, 4 ± 4).

Full Oral Feeding Phase

In the 48 hours after full oral feeding had been achieved (Table 4), the general pattern of the data within both groups was similar to that of their transition phase (Table 3). However, the experimental group's HF power increased in the postfeeding period producing a significant decrease in the LF/HF ratio compared with the LF/HF value in the feeding period.

When the two groups were compared after having completed their transition (Table 3), the statistical differences in all three HRV indices that existed between them in prefeeding of the transition period continued to exist (Table 4). Although only a small number of infants (control = 8, experimental = 3) still had feeding bradycardia during the full oral feeding period, control infants had significantly more bradycardia episodes (mean, 4 ± 3) compared with experimental infants (mean, 2 ± 1).

Discussion

Power Spectral Analysis

The spectral analysis of HRV provides a noninvasive and semiquantitative method of monitoring autonomic

Table 4. HRV Indices, Heart Rates, and Bradycardia Episodes During the Full Oral Feeding Phase

	10-Minute prefeeding*	During oral feeding	10-Minute postfeeding
Control infants (n = 41)			
HRV indices	**M (LCL–UCL)**	**M (LCL–UCL)**	**M (LCL–UCL)**
LF	9.31 (7.52–11.54)	8.42 (6.65–10.66)	9.27 (6.96–12.35)
HF	5.73 (3.87–8.47)	1.92 (1.37–2.68)**	4.29 (2.65–6.94)
LF/HF	1.61 (1.29–2.02)	4.44 (3.58–5.51)**	2.21 (1.67–2.92)**
	M ± SD	**M ± SD**	**M ± SD**
Heart rate	157 ± 3	156 ± 5	152 ± 5
Bradycardia	–	4 ± 3	–
Experimental infants (n = 37)			
HRV indices	**M (LCL–UCL)**	**M (LCL–UCL)**	**M (LCL–UCL)**
LF	5.92 (4.32–8.12)	9.00 (6.65–12.17)**	11.55 (8.44–15.82)
HF	2.45 (1.51–3.96)	2.89 (1.85–4.50)	6.51 (4.22–10.04)
LF/HF	2.40 (1.89–3.05)	3.06 (2.42–3.87)	1.79 (1.46–2.19)**
	M ± SD	**M ± SD**	**M ± SD**
Heart rate	153 ± 4	159 ± 5	154 ± 5
Bradycardia***	–	2 ± 1	–

HRV indices are expressed as squared milliseconds per Hertz and heart rates as bpm. M indicates geometric means for HRV indices (LF, HF, and LF/HF ratio), and arithmetic means for heart rates and bradycardia episodes; LCL–UCL, lower to upper confidence limit.

*LF, HF, and LF/HF are significantly different during the 10-minute prefeeding period ($P < .001$) between control and experimental groups.

**Indicates significant within-group differences for a 10-minute prefeeding to feeding period or a feeding to postfeeding period.

***Indicates significant differences ($P < .002$) between control and experimental groups.

function.[16,17] It is recognized that the LF power is predominately influenced by sympathetic activity (with some contribution from the parasympathetic system), whereas the HF power is predominately influenced by the parasympathetic system. Despite the many limitations of the method (identification and removal of artifacts, establishment of stationarity, and interpolation of missing beats), short-term recordings under controlled conditions give a reliable indication of the direction of change in autonomic balance.[18] In this study, HRV indices are objective physiological outcomes that serve to document the effects from two feeding conditions. The HRV indices provide a physiological rationale of greater complexity than the other outcomes (ie, time to attain feeding and behavioral responses).

Use of the Pacifier in the Prefeeding Period

Experimental infants who were given a pacifier before feeding had HRV indices that reflected less autonomic arousal than in the control infants (Table 3). The experimental infants had lower LF and HF power but higher LF/HF ratios than the controls. The higher LF/HF ratio was due to the disparity in the components of LF and HF power in the two groups. These differences continued after both groups were on full oral feeding for 48 hours (Table 4). It is worth noting that minute heart rate was relatively insensitive to these minute-to-minute changes in heart rate interval (heart rates between the two groups were similar throughout the study Tables 3 and 4). Our finding that nonnutritive sucking promotes vagal withdrawal and, to some extent, sympathetic inhibition is an explanation for the modulating effect that produced quiet awake behavior in the experimental infants compared with control infants.[6] It has been known for some time that use of pacifier sucking (nonnutritive sucking) has an alerting and quieting effect on infant behavior.[19,20] More recently, nonnutritive sucking during sleep in healthy term infants produced a modulation effect expressed as a lower sleep arousal threshold.[21]

Oral Feeding Period of the Transition Phase

The control infants showed an increase in the LF/HF ratio from the prefeeding period from 1.71 to 3.65, whereas the experimental infants did not change significantly (LF/HF 3.15–2.89), suggesting that the use of the pacifier and more frequent feeding opportunities provided by the semidemand protocol resulted in the autonomic balance of the experimental infants being more stable as they learned to feed.

During the 10-minute postfeeding period of the transition phase, the LF and HF increased and LF/HF decreased for infants in the control group from their feeding values, achieving values very similar to those of the experimental infants, whose LF and HF indices increased less so from their feeding values. The infants who were doing work during feeding were continuing to do work in the immediate postprandial period. In contrast to the voluntary work being done during feeding, the work being done in this immediate postprandial period was the physical and metabolic work of digestion. Both control and experimental infants had increases in HF and decreases in LF/HF ratios from the oral feeding period to the postfeeding period, indicating increased parasympathetic activity consistent with digestion. The similarity in the HRV indices in the 10 minutes after feeding indicates that both groups were digesting their nutrients in a normal manner. Assuming this is so, the values represent physiological values for autonomic activity in healthy preterm infants under postprandial conditions. Although not directly comparable to our study results because of differences in the measurement periods, Veerappan et al[5] also reported an increase in HF and a decrease in the LF/HF ratio 1 hour after feeding over prefeeding values among a healthy group of 34-week-PCA preterm infants.

Feeding Bradycardia

The prevalence of feeding bradycardia was similar in both study groups during the oral feeding period of the transition phase (Table 3). After the transition, bradycardia was more frequent in the control group than in the experimental group, with eight control infants continuing to have feeding bradycardia compared with only three experimental infants (Table 4). That the number of bradycardia episodes decreased after the infants achieved full oral feeding provides support for a learning effect being a factor in decreasing feeding bradycardia. The feeding bradycardia that persisted into the full oral feeding phase for the control infants may be due to immaturity in their coordination of sucking-swallowing-breathing. Because the experimental infants were offered oral feedings based on their readiness behavior, they had more opportunities (eight per day) to practice the coordination behavior. In comparison, the control infants were given gradual increases (from one to eight per day) in the frequency of scheduled feedings, and so they had fewer opportunities to practice, and their poor coordination persisted longer.

The HRV results of this study demonstrate that the use of the semidemand feeding protocol for easing the transition from gavage to oral feeding provided improvement in autonomic balance and stability for healthy preterm infants. The semidemand protocol that included the use of a pacifier before feeding and behavioral assessments to determine readiness to take oral feeding and to continue or terminate feeding, combined with the offering of maximum feeding opportunities, resulted in a smoother and more rapid transition to oral feeding than did standard care. Further study of how HRV changes with the transition from gavage to oral feeding for sicker preterm infants may help guide feeding strategies for these infants.

References

1. Sahni R, Schulze KF, Kashyap S, et al: Maturational changes in heart rate and heart rate variability in low birth weight infants. Dev Psychobiol 37:73–81, 2000
2. Chatow U, Davidson S, Reichman BL, et al: Development and maturation of the autonomic nervous system in premature and full-term infants using spectral analysis of heart rate fluctuations. Pediatr Res 37:294–302, 1995
3. McCain GC, Gartside PS, Greenberg JM, et al: A feeding protocol for healthy preterm infants that shortens time to oral feeding. J Pediatr 139:374–379, 2001
4. DiPietro JA, Cusson RM, Caughy MO, et al: Behavioral and physiologic effects of nonnutritive sucking during gavage feeding in preterm infants. Pediatr Res 36:207–214, 1994
5. Veerappan S, Rosen H, Craelius W, et al: Spectral analysis of heart rate variability in premature infants with feeding bradycardia. Pediatr Res 47:659–662, 2000
6. McCain GC, Gartside PS: Behavioral responses of preterm infants to a standard-care and semi-demand feeding protocol. Newborn Infant Nurs Rev 2:187–193, 2002
7. Akselrod S, Gordon D, Ubel FA, et al: Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. Science 213:220–222, 1981
8. Burr RL, Anderson ST, Downs WG: Biophysical measurement series. Redmond (Wash): Space Labs, 1992
9. Mehta SK, Super DM, Connuck D, et al: Heart rate variability in healthy newborn infants. Am J Cardiol 89:50–53, 2002
10. Patzak A, Lipke K, Orlow W, et al: Development of heart rate power spectra reveals neonatal peculiarities of cardiorespiratory control. Am J Physiol 271:R1025–R1032, 1996
11. Eiselt M, Curzi-Dascalova L, Clairambault J, et al: Heart-rate variability in low-risk prematurely born infants reaching normal term: a comparison with full-term newborns. Early Hum Dev 32:183–195, 1993
12. Curzi-Dascalova L: Physiological correlates of sleep development in premature and full-term neonates. Neurophysiol Clin 22:151–166, 1992
13. Pocock SJ, Simon R: Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. Biometrics 31:103–115, 1975
14. McCain GC: An evidence based guideline for introducing oral feedings to healthy preterm infants. Neonatal Netw 22:45–50, 2003
15. Rosen H, Craelius W, Curcie D, et al: Spectral analysis of heart variability in the newborn infant. Biol Neonate 77:224–229, 2000
16. Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology: Heart rate variability standards of measurement, physiological interpretation, and clinical use. Circulation 93:1043–1065, 1996
17. Pumprla J, Howorka K, Groves D, et al: Functional assessment of heart rate variability: physiological basis and practical applications. Int J Cardiol 84:1–14, 2002
18. Lombardi F: Clinical implications of present physiological understanding of HRV components. Card Electrophysiol Rev 6:245–249, 2002
19. Gill NE, Behnke M, Conlon M, et al: Effect of nonnutritive sucking on behavioral state in preterm infants before feeding. Nurs Res 37:347–350, 1988
20. McCain GC: Facilitating inactive awake states in preterm infants: study of three interventions. Nurs Res 41:157–160, 1992
21. Franco P, Scaillet S, Wermenbol V, et al: The influence of a pacifier on infants' arousals from sleep. J Pediatr 136:775–779, 2000