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Maternal Voice and Short-Term Outcomes in Preterm Infants

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Abstract

This study explored effects of exposure to maternal voice on short-term outcomes in very low birth weight preterm infants cared for within an neonatal intensive care unit (NICU) without an ongoing program of developmental care. Using a comparative design, 53 infants born during their 27th to 28th postmenstrual week were sampled by convenience. Experimental groups were exposed to maternal voice during two developmental time periods. Group 1 listened to a recording of their mothers reciting a rhyme from 28 to 34 postmenstrual weeks. Group 2 waited 4 weeks and heard the recording from 32 to 34 weeks. The control group received routine care. The primary analysis of combined experimental groups compared to the control group revealed that the experimental infants experienced significantly fewer episodes of feeding intolerance and achieved full enteral feeds quicker compared to the control group. Further, in an analysis evaluating all three groups separately, it was noted that Group 1 experienced significantly fewer episodes of feeding intolerance compared to the control group. Study findings warrant further investigation of exposure to maternal voice and the developmental timing at which exposure is begun.

Keywords

development; maternal; auditory stimulation; neonatal intensive care unit; preterm infant

INTRODUCTION

Transitions in interactions between genetic, physiological, behavioral, and environmental factors occurring during the final trimester of fetal gestation and early preterm infant development necessitate sensitivity to how these transitions change over time (Gottlieb, 1992; Lickliter, 2000). Hence, consideration for developmental timing is a key component of developmental care programs directed toward improving outcomes in preterm infants. Attention to when interventions are begun is needed, due to significant neurobehavioral advances that culminate with functional maturity of the autonomic nervous system at approximately 32 weeks postmenstrual age (PMA) for preterm infants (Groome, Loizou, Holland, Smith, & Hoff, 1999; Groome et al., 1999; Holmes, 1986). Cohorts of infants younger than 32 weeks may therefore be affected differently by interventions compared to infants greater than 32 weeks PMA. For example, increased family involvement in conjunction with developmental care is encouraged and has been shown to positively influence short-term outcomes in preterm infants (Als et al., 2003; Melnyk et al., 2006; Zeskind & Iacino, 1984). The amount of parental touching and talking to their infants', however, is varied depending upon the infant's individual response and developmental age (Butler & Als, 2008; Gibbins, Hoath, Coughlin, Gibbins, & Frank, 2008).

Exposure to voice recordings of the infants' mother is currently not included in programs of developmental care. While previous studies have demonstrated potentially positive effects on short-term outcomes, few of the findings reached statistical significance and all used sound levels above current recommendations (hourly L_{eq} of 50 dB; hourly L_{10} of 55 dB; and 1-s duration $L_{max} < 70$ dB)¹ established by the American Academy of Pediatrics Committee on Environmental Health (1997; Graven, 2000). In addition, all studies played maternal recordings to cohorts of infants whose developmental age bridged a time period when significant neurobehavioral advances in the auditory and autonomic nervous systems are occurring (Krueger, in press). The purpose of this study was to explore the effects of exposure to maternal voice recordings (using recommended sound levels) initiated during two developmental time periods (<32 weeks' PMA and 32 weeks PMA) on short-term outcomes in very low birthweight infants born during their 27th to 28th postmenstrual week.

DEVELOPMENTAL CARE AS A METHOD TO IMPROVE SHORT-TERM OUTCOMES

Developmental care is a program of interventions that provides individualized care based on the age and health status of the preterm infant. By paying attention to individual differences in health status and developmental age, this program of care has been shown to advance short-term outcomes in preterm infants and has produced improvements or decreases in the length of infant hospital stays (Als et al., 2003; Jacobs, Sokol, & Ohlsson, 2002; McNulty et al., 2009; Westrup, Kleberg, von Eichwald, Stjernqvist, & Lagercrantz, 2000). Through instituting a program of developmental care, Als et al. (2003) found that very low birth weight (VLBW) infants required significantly fewer days of mechanical ventilation and supplemental oxygen support, tolerated earlier oral feedings, experienced improved daily weight gain, and required a shorter hospital stay. This was further supported by a retrospective chart review in which fewer episodes of feeding intolerance after implementation of a developmental care program were noted (Prentice & Stainton, 2003).

Westrup et al. (2000) investigated the effects of developmental care on the amount of respiratory support required by preterm infants. Compared to those receiving routine neonatal intensive care unit (NICU) care, significantly fewer days on nasal continuous positive pressure (CPAP) were noted (26.1 days vs. 43.9 days; $p = .045$), and these infants were discharged at a younger age (33 weeks vs. 38.1 weeks). Reduced need for respiratory support following implementation of developmental care was further supported by findings from a meta-analysis of five randomized control trials (Jacobs et al., 2002). By decreasing the time to achievement of oral feeding and percentage of time spent on respiratory support, these studies suggested that provision of developmental care to preterm infants may ultimately reduce length of time to discharge.

FAMILY INVOLVEMENT AND SHORT-TERM OUTCOMES

Another factor positively influencing an infant's length of stay in the NICU is family involvement. While it was not clear whether the NICU at the study site had an organized program of developmental care or the age range of the preterm participants, Melnyk et al. (2006) evaluated the use of an educational-behavioral intervention program designed to increase parent-infant interaction. It was found that infants whose parents were involved in this program had a shorter NICU stay (31.9 days vs. 35.6 days). Similarly, Zeskind and Iacino (1984) showed that more frequent maternal visitation significantly decreased length of hospitalization in preterm infants by 8 days ($p < .001$). Little is known, however, about

¹The L_{eq} is the equivalent steady decibel (dB) level across a given sample or time period. The L_{10} is a measure of the decibel level exceeded for 10% of the hour; the L_{max} is the highest decibel level measured for at least 1/20th second duration during the hour.

the potential effect of exposure to maternal voice recordings (independent of visitation) on short-term outcomes.

Mother's Voice

The cochlea and peripheral sensory end organs are structurally complete as early as the 24th prenatal week warranting attention to sound and its effects on the developing preterm infant (Philbin, 2000). Studies investigating reintroduction of the mother's voice using recordings played to preterm infants have documented some effects but are largely historical. They were all conducted with what we know today to be unsafe sound levels or greater than 50–55 dB (Graven, 2000) and were not guided by a developmental framework in terms of at what age exposure to the maternal voice recordings was begun (Krueger, in press).

In a cohort of 26- to 33-week PMA infants, Chapman (1978) and Malloy (1979) studied effects of daily exposure to a taped recording of maternal voice (Group 1), an orchestra playing Brahms' *Lullaby* (Group 2), and routine NICU care (control group). Recordings were played to preterm infants at 70–75 dB. Chapman reported a clinically relevant finding that infants exposed to their mothers' voices demonstrated the gross motor pattern of laterality (preference for use of one side) more (68%) than those listening to the lullaby (58%) and those in the control group (50%). In a follow-up study with the same infants, Malloy evaluated weight gain and developmental outcomes at 1 day following discharge and at 9 months of age using components of Rosenblith's Behavioral Examination of the Neonate and Bayley Scales of Infant Development (Bayley, 1969; Malloy, 1979; Rosenblith, 1961). No statistical between-group differences were noted.

Two more recent studies have reported advantages of exposure to maternal voice, but none were significant. Standley and Moore (1995) compared effects of exposure to maternal voice and music on preterm infants. PMA of these infants was not indicated, but they were referred to as preterm and 14–16 days postbirth. Infants were exposed to 20-min recordings of either maternal voice or music (decibel level = 65–70) for three consecutive days. While researchers found that both maternal voice and music positively affected mean percent oxygen saturation rates, only the music group displayed significantly higher oxygen saturation rates on Days 2 and 3 ($p < .05$). Findings suggested that exposure to maternal voice does not stabilize infants' oxygen regulation as well as music.

In the most recent study, Johnston, Filion, and Nuyt (2007) examined a mix of preterm and late preterm infants delivered between 32 and 36 weeks gestational age, during a routine painful procedure in the NICU (heel stick). Infants were tested 10 days after birth following a 48-hr exposure to hearing their mothers' voices three times a day. Recordings were presented for 10 min at 70 dB and filtered, in order to mimic how the mother's voice sounds from within the amniotic fluid of the uterus. Outcomes measured were components of a pain tool (oxygen saturation, facial expressions, and sleep–wake state). No significant beneficial findings were reported; however, a significantly greater decrease in oxygen saturation rates ($p < .01$) was noted following exposure to maternal voice (94.1%) compared to no exposure prior to the heel stick (96.2%). In response to this negative effect for exposure to maternal voice, the authors noted the sound level for the maternal recording (70 dB) was greater than recommended levels of 50–55 dB (Graven, 2000) and questioned whether using such high levels was aversive to the infant.

Inconclusive findings as to whether exposure to maternal voice affects short-term outcomes in preterm infants may be due to use of unsafe sound levels and lack of attention to the developmental timing at which exposure is begun. The study reported here was therefore designed with attention to developmental timing in order to explore the potential impact of exposure to maternal voice on short-term outcomes using safe sound levels and during two

developmental time periods (either from 28 to 34 weeks' PMA or 32 to 34 weeks' PMA) in preterm infants born during their 27th to 28th postmenstrual week.

METHODS

Setting and Sample

Using a comparative design, this study was initiated as part of a larger quasi-experimental study entitled, Heart Rate Variability and Learning in the 28–34 Week Old Preterm. Fifty-four infant participants were recruited from a Level 3 NICU located in the southeastern United States. During the study period, only one protocol involving developmental care was instituted in this particular NICU: minimal stimulation with a particular focus on provision of clustered care (provided all routine care during designated periods of time to allow for increased periods of rest) (Symanski, Hayes, & Akilesh, 2002).

All infants were born between 27 and 28 weeks PMA and began participation in the study during 28 weeks' PMA. PMA was determined from the mothers' last menstrual period. Exclusion criteria consisted of the following: (1) abnormal head ultrasound, (2) sensorineural hearing loss, (3) confirmed prenatally transmitted viral/bacterial infections, (4) cardiac abnormalities, and (5) diagnosed abdominal disorder.

Following parental informed consent, 34 experimental infants were randomly assigned in blocks of four to one of two experimental groups (SAS Software, v9.1.3, Cary, NC). Group 1 infants ($n = 16$) listened to a CD recording of a nursery rhyme recited by their mothers twice a day from the 28th to 34th week PMA; Group 2 infants ($n = 17$) listened from the 32nd to 34th week. Twenty control group infants were retrospectively obtained via a chart review of infants in the NICU during the study's experimental condition.

The mean maternal age was 24.8 years (range: 18–41). Sixty percent of mothers reported Caucasian ethnicity, 38% African American, and 2% Hispanic. Mean infant birth weight was 1091.3 ± 203.9 g. Forty-two percent were males; 58% percent were females. The mean Neurobiological Risk Score (NBRS) collected on each was 2.98. The NBRS is a scale assigning points from 0 to 4 for various neonatal conditions correlated with adverse developmental outcomes (Brazy, Eckerman, Oehler, Goldstein, & O'Rand, 1991). See Table 1 for demographic information by group assignment.

Independent Variable

A CD recording of the mother reciting a nursery rhyme was used in the experimental component of this study. The untitled rhyme (Simon & Schuster, 1985) was nine lines long, took approximately 15 s to recite, and was not a common verse, making it unlikely that infants would be spontaneously exposed to it. Recordings of the rhyme were made by asking mothers to use infant-directed speech or motherese, a method of verbalization that emphasizes greater pitch changes and slower speech. Although the effect of motherese on preterm infants is unknown, newborns have been shown to systematically prefer human speech with these characteristics (Cooper & Aslin, 1994).

Recordings lasted approximately 45 s and were played twice a day over a 12.5-cm speaker positioned 20 cm from the infant's ear. Sound levels were measured using an A-scale of a Bruel-Kjaer (220SLM) sound level meter. Overall stimulus intensity was 50–55 dB (mean = $53.9; \pm 2.35$ dB), with sound levels within the infants' cribs just prior to initiation of recordings ranging between 48.6 and 69.2 dB (mean = 57.90 ± 4.01 dB). Fifty to fifty-five decibels was chosen in order to maintain the decibel level just below the normal level of human speech (58–60 dB) (Gerhardt, 1989) and to remain within recommended sound levels for the preterm infant (Graven, 2000).

Short-Term Outcomes

Charts for all infants in experimental and control conditions were reviewed by a neonatal nurse practitioner to obtain short-term outcomes. Data retrieval was initiated at >95% interrater reliability and maintained at the same by evaluating 10% of the charts on completion.

Number of Days to Discharge—Defined as the number of days from birth to the infant's discharge home or transfer to another facility.

Average Daily Weight Gain—The total weight gained (in grams) divided by the number of days cared for within the NICU.

Days to Full Enteral Feedings—The number of days from birth to tolerance of 120 ml/kg the day of feedings.

Number of Days to Full Oral Feeding—Defined as tolerance of all feedings via breast or bottle.

Episodes of Feeding Intolerance—A single episode of feeding intolerance was defined as the presence of gastric residuals equal or greater than 3 ml/kg (Mihatsch et al., 2002). The definition of feeding intolerance varies among institutions and individual clinicians. Generally, it includes the presence of gastric residuals and has been found to be positively associated with a delay in attainment of full enteral feedings and decreased weight gain (Akintorin, Kamat, Pildes, Kling, & Andes, 1997).

Days NPO—This was defined as the number of days infants were fed nothing per oral administration (NPO) for at least 50% of a 24-hr period due to events other than routine preparation for a procedure or intervention.

Percent Days on Respiratory Support—Respiratory support in the NICU includes ventilation (conventional ventilation and high-frequency ventilation), CPAP, and supplemental oxygen (delivered via high flow nasal cannula, conventional nasal cannula, or oxyhood). Chart reviews were conducted for each infant to obtain number of days on supplemental oxygen [nasal cannula (NC), high flow nasal cannula (HFNC), and oxyhood], nasal CPAP, and ventilator support (conventional ventilation and high-frequency ventilation). A summary statistic was then created (percent days on respiratory support) by taking the total number of days on any form of respiratory support (supplemental oxygen, CPAP, or ventilation) and dividing it by total days cared for in the NICU.

Procedure

Experimental Condition—Maternal CD recordings were played while experimental infants remained in assigned NICU incubator beds. Recordings were played twice a day (between 8 AM and 8 PM) with the infant in an active sleep state. Either maternal recordings were begun at 28 weeks of age (Group 1) and played daily until 34 weeks or the infant waited until 32 weeks of age (Group 2), and the maternal recordings were played daily until 34 weeks. In order to ensure infants' consistent sleep-wake state while recordings were played, behavioral responses (irregular respirations, eyes open or closed, body movements) were monitored and recorded onto a maternal log just prior to and while each recording was played.

The active sleep state was selected for use in this study because preterm infants spend the most time in this behavioral state, making it more likely that recordings were played while

infants were in a consistent sleep–wake state. Behavioral criteria used to determine subjects were in an active sleep state were as follows: (1) irregular respirations, (2) presence of no body movement, and (3) eyes closed (Holditch-Davis, 1990; Holditch-Davis, Scher, Schwartz, & Hudson-Barr, 2004; Thoman, 1990). Interrater reliability in behavioral state detection was maintained at 90% agreement.

Control Group Condition—Control group infants were also born during their 27th to 28th postmenstrual week but did not undergo either of the experimental conditions. All control infants were cared for in the NICU during the same time period the experimental condition of this study was conducted.

Data Lost

Of the 54 participants initially enrolled, one from Group 1 was excluded from analysis because the infant was diagnosed with duodenal atresia following enrollment. For one control infant, a complete medical record could not be located, leaving this infant's demographic information unavailable. Information related to short-term outcomes for this control infant, however, was retrieved and included in the analysis.

Statistical Analyses

All data were analyzed using the SAS (v 9.1.3). Descriptive statistics (frequencies, percentages, means, standard deviations) were determined to characterize the sample. Two methods of analysis were used to evaluate our hypotheses. First, two-sample *t*-tests were used to evaluate differences between the combined experimental groups (Groups 1 and 2) and the control group. Second, ANOVAs were conducted including data from all three groups separately. For these analyses, if the overall ANOVA was significant we performed between-group multiple comparisons (Group 1 vs. Group 2; Group 1 vs. controls, Group 2 vs. controls) after applying Bonferroni correction to ensure an overall error rate of .05. Significant results from these pair-wise comparisons are reported as $p < .05$.

RESULTS

Overall *t*-test comparisons of short-term outcomes are listed in Table 2. A comparison of the combined experimental group to the control group revealed significant differences in episodes of feeding intolerance ($F = 7.5$; $df = 1,45$; $p < .01$) and days to full enteral feeds ($F = 5.5$; $df = 1,38$; $p < .02$). A three-group ANOVA for feeding intolerance was also significant ($F = 3.69$; $df = 2,44$; $p < .03$). After applying a Bonferroni correction, it was noted that Group 1 experienced significantly fewer episodes of feeding intolerance in comparison to the control group ($p < .05$). While overall comparisons of other outcome parameters were not significant it should be noted that, due to larger than expected variability in the data, the comparisons were under-powered.

DISCUSSION

Taking together the positive effects of increased family involvement in conjunction with developmental care on short-term outcomes in preterm infants (Als et al., 2003; Butler & Als, 2008; Gibbins et al., 2008; Melnyk et al., 2006; Zeskind & Iacino, 1984) and previous equivocal and historical studies investigating the effect of exposure to maternal voice (Chapman, 1978; Johnston et al., 2007; Malloy, 1979; Standley & Moore, 1995), our findings suggest that infants exposed to a recording of maternal voice (combined experimental) experienced improved short-term outcomes compared to infants receiving routine NICU care (control group). Infants in the combined experimental group experienced significantly fewer episodes of feeding intolerance and achieved full enteral feeds in fewer

days. Further, using a Bonferroni correction for pair-wise comparisons between outcomes for Group 1, Group 2, and the control group (employing sound levels within current recommendations for auditory stimulation provided to the preterm infant) a potential significant advantage for beginning exposure before 32 weeks' PMA (Group 1) was noted in relation to episodes of feeding intolerance.

Findings for both experimental groups are consistent with those reported by Akintorin et al. (1997), in which decreased numbers of episodes of feeding intolerance were associated with earlier attainment of full enteral feeds. Both groups of experimental infants experienced fewer episodes of feeding intolerance and achieved full enteral feeds earlier than the control group who received routine NICU care.

Differences between groups regarding the percentage of days on respiratory support are consistent with studies demonstrating a reduction in the level of respiratory support while participating in a program of developmental care (Jacobs et al., 2002; Westrup et al., 2000) and call attention to the need for attention to developmental timing. These variations related to the developmental timing at which exposure to maternal voice is begun can also be seen in other variables noted in Table 2. For example, while not statistically significant, Group 2, who experienced exposure to maternal voice from 32- to 34-week PMA, experienced the smallest percentage of days on some level of respiratory support. However, for Group 1, who experienced the earliest and longest exposure to maternal voice from 28- to 34-week PMA, the overall level of respiratory support is the highest (see Tab. 2). Even though a consistent program of developmental care was not in place for infants participating in the present study, the finding for Group 2 is consistent with previous research investigating beneficial effects of developmental care (Als et al., 2003; Jacobs et al., 2002; Westrup et al., 2000). The finding that Group 1 experienced the highest percentage of days on respiratory support, however, suggests that earlier and longer exposure to maternal voice for Group 1 may not have been advantageous in all areas of development and warrants future research with attention to developmental timing.

Caution is needed when interpreting the results due to limitations related to the study sample. The sample was limited by an imbalance between group sample size which reduced statistical power, by greater than expected variability in the data, and an imbalance in the number of days infants received breast milk feedings. With regard to this last point, the imbalance between groups may be attributed, in part, to attrition to outside hospitals and death of the infant prior to discharge readiness. Further, experimental infants received breast milk for a higher number of days compared to control group infants but the difference was not significant ($p = .19$). Provision of breast milk to VLBW infants, however, has been associated with decreased feeding intolerance (Sisk, Lovelady, Gruber, Dillard, & O'Shea, 2008). Due to the wide range of variability on the days full breast milk was received (see Tab. 1), it was not concluded that this factor confounded the findings presented here. control for days fed breast milk, however, warrants attention as a potential confounding factor in future studies.

Additional design limitations included use of a retrospective chart review, use of only exposure to maternal voice recordings, variability in outcome measures due to variation in clinician decisions related to advancement of nutritional, and respiratory milestones while preterm infants are cared for within the NICU, and that our NICU did not have an organized program of developmental care. A retrospective chart review leaves the researcher dependent upon others for collection of data thus, reducing reliability of the data. Further, infants participating in this study were only exposed to a low-level, repeated recording of the maternal voice. Given the positive beneficial effects following exposure to music (Standley & Moore, 1995), future studies using other low-level auditory events are needed.

Subjective variations in clinician decisions related to advancement of enteral or oral feedings, use of respiratory support, and discharge readiness contribute to variability and thus the rendering of nonsignificant results. This is, however, an unavoidable situation in that decisions to initiate, continue, or discontinue respiratory support are often based on individual clinical opinion rather than specific guidelines. Finally, although our NICU did not have an organized program of developmental care, nurses and clinicians were potentially affected by scientific reports related to benefits of such a program and may have inconsistently employed some interventions on their own, at random. Despite these limitations, it is important to note that both statistical and potential clinically relevant outcomes were noted for participation in the experimental groups, suggesting that exposure to maternal voice does promote improvement in short-term outcomes for preterm infants.

SUMMARY

Delays in achievement of nutritional and respiratory milestones are associated with increased incidence of nosocomial infection, family stress, and hospital costs (Macey & Harmon, 1987; Shaw et al., 2006; St. John, Nelson, Cliver, Bishnoi, & Goldenberg, 2000). Increased family involvement in conjunction with developmental care is encouraged and has been shown to positively influence short-term outcomes in preterm infants (Als et al., 2003; Butler & Als, 2008; Gibbins et al., 2008; Melnyk et al., 2006; Zeskind & Iacino, 1984). Findings reported here underscore the need for further study of the potential for an inexpensive intervention—exposure to a recording of mother's voice—to enhance achievement of these critically important short-term outcomes while controlling when in development the recordings are begun.

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Table 1

Demographic Characteristics

	Primary Analysis Groups			
	Group 1 (n = 16)	Group 2 (n = 17)	Combined (n = 33)	Control (n = 19)
Maternal characteristics				
Age (year)	22.31 ± 4.36	28.24 ± 7.34	25.36 ± 6.70	23.74 ± 4.64
Ethnicity				
White	69%	59%	64%	53%
African American	31%	35%	33%	47%
Hispanic	—	6%	3%	—
Mode of delivery				
Vaginal	50%	18%	33%	37%
Cesarean section	50%	82%	67%	63%
Infant characteristics				
Gender				
Male	25%	53%	39%	47%
Female	75%	47%	61%	53%
Birth weight (g)	1104.9 ± 148.7	1055.6 ± 256.5	1079.5 ± 209.5	1111.6 ± 197.8
APGAR score				
1 min	6.37 ± 1.71	5.29 ± 2.47	5.82 ± 2.17	4.79 ± 2.86
5 min	7.34 ± 1.41	7.41 ± 1.28	7.42 ± 1.32	7.11 ± 1.70
NBR ^S ^a	2.44 ± 2.0	3.25 ± 2.79	2.94 ± 2.42	3.2 ± 3.09
Days mother visited	4.42 ± 1.84	3.95 ± 1.52	4.17 ± 1.66	2.96 ± 1.83
Days full breast milk ^b	22.81 ± 20.77	18.93 ± 18.59	20.94 ± 19.51	13.12 ± 17.90
Days full formula ^c	15.44 ± 17.53	19.87 ± 20.21	17.58 ± 18.69	28.56 ± 23.99
Days mixed ^d	2.57 ± 3.10	7.0 ± 9.86	4.71 ± 7.44	1.38 ± 2.25
Incidence of NEC ^e	31%	19%	25%	30%

Note. For one control infant the complete medical record could not be located, leaving this infant's demographic information unavailable.

^aNeurobehavioral risk score.

^bOnly breast milk consumed in a 24-hr period.

^cOnly formula consumed in a 24-hr period.

^dReceived both formula and breast milk in a 24-hr period.

^eBoth suspected and diagnosed NEC.

Table 2

Short-Term Outcomes: Mean ± SD

Outcomes	Primary Analysis Groups				
	Group 1 (n = 16)	Group 2 (n = 17)	Combined Experimental (n = 33)	Control (n = 20)	p-Value (t-Test)
Wt gain ^a	20.46 ± 5.01	18.77 ± 10.16	19.59 ± 8.01	18.07 ± 10.89	.57
Days to D/C	56.8 ± 20.8	53.9 ± 23.5	55.3 ± 21.9	52.2 ± 24.7	.64
Days NPO ^b	9.6 ± 7.74	7.7 ± 9.05	8.63 ± 8.3	10.11 ± 7.18	.52
Days to full enteral feeds ^c	28.9 ± 13.6	25.5 ± 9.0	27.32 ± 11.64	38.5 ± 18.1	.02

Outcomes	Primary Analysis Groups				
	Group 1 (n = 15)	Group 2 (n = 13)	Combined Experimental (n = 28)	Control (n = 12)	p-Value (t-Test)
Days to full oral feeds	59.9 ± 6.1	51.3 ± 17.4	55.06 ± 13.98	51.3 ± 12.7	.50

Outcomes	Primary Analysis Groups				
	Group 1 (n = 7)	Group 2 (n = 9)	Combined Experimental (n = 16)	Control (n = 10)	p-Value (t-Test)
Feeding intolerance ^d	2.8 ± 2.62	3.1 ± 3.18	2.94 ± 2.86	6.4 ± 5.81	.009
Overall resp. support ^e	.64 ± .29	.51 ± .33	.57 ± .31	.60 ± .42	.80

Note. Sample size variation related to full enteral and full oral feeds is noted above because not all infants achieved these outcomes during their hospital stay.

^aMean daily weight gain.

^bNo feedings for >50% of a 24-hr period.

^cDays to achieving 120 ml/kg/day feedings.

^dOver 3 ml/kg/day gastric residuals or feedings held.

^ePercent of days on supplemental oxygen, CPAP, or ventilation.