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# Implementation of Feeding Guidelines Hastens the Time to Initiation of Enteral Feeds and Improves Growth Velocity in Very Low Birth-Weight Infants

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**ABSTRACT**

**Background:** Growth and nutrition are critical in neonatal care. Whether feeding guidelines improve growth and nutrition and reduce morbidity is unknown.

**Purpose:** Feeding guidelines for very low birth-weight (VLBW) infants were implemented in our neonatal intensive care unit (NICU) to start and achieve full enteral feeds sooner, and increase weight gain over the first month.

**Methods:** Feeding guidelines for VLBW infants were implemented in January 2014, stratified by birth weight (<750, 750-1000, and 1000-1500 g). After trophic feedings, enteral feedings were advanced by 20 to 30 mL/kg/d.

Data were analyzed for 2 years prior (baseline) and 6 months after (guideline) guidelines were implemented and included days to initiation of enteral feeds, days on total parenteral nutrition (TPN), and weight gain over the first month. Potential concomitant factors that could affect feeding tolerance were examined including indomethacin or dopamine treatment, delivery room cardiopulmonary resuscitation, and growth restriction.

**Results:** A total of 95 infants with a birth weight of less than 1500 g were included (59 baseline and 36 guideline). Days to start enteral feeds decreased by 47% ($P < .01$) and days on TPN decreased by 25% (16 days vs 11 days; $P < .01$). Weight gain over the first month of life increased by 15% ($p < .05$). Dopamine and indomethacin use decreased during the study period, and small for gestational age infants were overrepresented in the guideline group.

**Implications for Practice/Research:** Establishment of feeding guidelines for VLBW infants in our NICU reduced the days to start feeds and days on TPN while increasing weight gain over the first month. Improving growth and nutrition and reducing need for TPN in this vulnerable population may ultimately prevent infection and improve neurodevelopmental outcomes.

**Key Words:** feeding guidelines, neonatal growth, neonatal intensive care unit (NICU), neonatal nutrition, very low birth weight (VLBW)

## BACKGROUND AND SIGNIFICANCE

Studies have shown that standardization of feeding practices for preterm infants improves growth, decreases cost by reducing parenteral nutrition use, and reduces the incidence of late-onset sepsis.[1-3] In addition, a standardized approach to feeding preterm infants has been shown to reduce the incidence of necrotizing enterocolitis (NEC), which is a major contributor to death and long-term morbidity in this population.[2,4-6] Because of advances in the care of preterm infants, there is increased survival, but with an increase in secondary morbidities including respiratory disease, feeding difficulties, and neurologic handicaps.[7] Thus, the provision of adequate growth and nutrition is a critically important facet of the care of preterm infants.[1,8]

Strong evidence suggests that early feedings, known as trophic feeds, are a safe way to promote postnatal gastrointestinal maturation, and when compared with delayed enteral feeding, provide benefit to this vulnerable population.[9-11] The rate of advancement of enteral feedings in very low birth-weight (VLBW) infants is controversial, as too rapid an advance has been associated with an increased risk of NEC.[12] Other studies have demonstrated that advancement of enteral feeds by 30 mL/kg/d is safe and does not increase the incidence of NEC compared with more conservative approaches.[13-17] By advancing feeds at a

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slightly faster rate, VLBW infants regain birth weight quicker, have less need for total parenteral nutrition (TPN), and have decreased length of stay.[13-17] Certain factors, including intrauterine growth restriction (IUGR), presence of a patent ductus arteriosus (PDA), and treatment with indomethacin, may adversely affect intestinal blood flow and increase the risk of feeding intolerance and NEC.[18,19] Furthermore, hemodynamic instability requiring vasopressor support is considered by many neonatologists to be a relative contraindication to enteral feeding. These factors should be considered when establishing feeding guidelines for these fragile infants.

In an effort to improve nutrition and growth outcomes and to reduce secondary morbidity, we designed a quality improvement (QI) project to standardize the initiation and approach to feeding VLBW infants in our neonatal intensive care unit (NICU). The 2 primary aims of the project were to (1) initiate enteral feedings earlier in the infant's clinical course, and (2) achieve full enteral feedings faster. The purpose of these aims was to decrease the need for TPN, and to improve weight gain specifically over the first month of life in our VLBW infants. Because clinical factors such as the presence of a PDA or need for low-dose vasopressor support may cause reluctance of neonatal providers to initiate enteral feedings, we addressed these factors with implementation of the guidelines. In addition, the impact of congenital anomalies on feeding initiation and tolerance in VLBW infants has not been well described, so these patients in our tertiary referral NICU were included in the QI initiative.

### What This Study Adds

- Standardized approach to feeding VLBW infants reduces time to full enteral feedings and reduces TPN days, which may reduce morbidity in preterm infants.
- Close attention to enteral feeding improves growth over the first month of life, which may have long-term implications related to neurodevelopment.
- A multidisciplinary team approach helps facilitate implementation of standardized feedings guidelines and the provision of optimal nutrition in preterm infants.

## METHODS

Feeding guidelines for VLBW infants were developed after an extensive review of the literature[2,5,13,15,16,20-24] and a consensus conference including neonatal physicians, neonatal nurse practitioners, nurses, and neonatal registered dieticians practicing in our NICU. The guidelines were developed in collaboration with our local affiliated NICU, where they were first implemented in 2012.[25]

The guidelines were stratified by birth weight in grams (<750, 750-1000, and 1000-1500 g), as gestational age is often unknown or unreliable (Figure 1). Infants begin with trophic feeds of less than or equal to 20 mL/kg/d on the first day of feedings, and feedings were subsequently advanced by 20 to 30 mL/kg/d. A more conservative advancement of feeds (eg, 20 mL/kg/d vs 30 mL/kg/d) was recommended in the presence of specific perinatal and neonatal risk factors. Those included umbilical cord gas or infant's first gas with significant metabolic acidosis (pH <7 and base deficit >15), asymmetric IUGR, IUGR with absent end diastolic flow, and monochorionic twin gestation with twin–twin transfusion syndrome. Neonatal risk factors include significant cardiovascular instability (defined as history of chest compressions, vasoactive agent requirement, or multiple crystalloid or colloid fluid boluses), symptomatic PDA, and prolonged nil per os (NPO) status greater than 7 days.

Early enteral feedings were encouraged regardless of indomethacin therapy and presence of an umbilical arterial catheter, and maternal or donor breast milk was strongly encouraged for all feedings. Fortification to 22 kcal/oz was recommended after enteral feeds reached 80 mL/kg/d. Fortification beyond 22 kcal/oz was left to provider discretion and typically occurred after infants reached full enteral feeds of 150 to 160 mL/kg/d at our institution.

These feeding guidelines were then implemented in January 2014, after comprehensive staff education in our 82-bed academic Level IV NICU of primarily outborn infants. They were discussed during daily patient rounds and compliance encouraged by dedicated NICU registered dieticians. Bedside nurses played a crucial role as they reported each infant's response to feeding on a daily basis. The method and interval of feeding was left to the discretion of the treatment team.

Data were retrieved for 2 years prior (baseline group: 2012-2013) and 1 year after implementation of the guidelines (guideline group: 2014) using EPIC, an online medical record system. Two years of baseline data were analyzed to allow for better statistical analysis. Data from year after implementation were felt to be adequate to address the short-term outcomes. Inclusion criteria were birth weight less than 1500 g and if enteral feedings had not been initiated before admission. The guidelines were used for all VLBW infants in our unit, but for accuracy of data analysis only infants who had not been fed before admission were included. Infants with congenital anomalies were not excluded from this study as to better represent the population of NICU patients at tertiary referral NICUs.

Data analysis included day of life at initiation of enteral feeds, total days on TPN, and growth velocity over the first month (defined as grams/kilogram/day). Total days on TPN were collected as a surrogate for time to full enteral feeds as this information

FIGURE 1

| Weight (g) | DOF* 1 | DOF 2 | DOF 3 | DOF 4 | DOF 5 | DOF 6 | DOF 7 | DOF 8 | DOF 9 | DOF 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| ≤750 | ≤20 | ≤20 | ≤20 | ≤20 | ≤20 | ≤50 | ≤80 Fortify | ≤110 | ≤140 | 160 |
| 750-1000 | ≤20 | ≤20 | ≤20 | ≤50 | ≤80 Fortify | ≤110 | ≤140 | 160 | | |
| 1000-1500 | ≤20 | ≤20 | ≤50 | ≤80 Fortify | ≤110 | ≤140 | 160 | | | |

*DOF = day of feed

**Risk Factors supporting conservative advancement of feeds:**

Perinatal:

1) Umbilical Cord Gas or infant's first blood gas with metabolic acidosis: *pH <7 and base deficit >-15*
2) Asymmetric IUGR or IUGR with reversed or absent end-diastolic flow
3) Monochorionic twin gestation with Twin-Twin Transfusion Syndrome

Neonatal:

1) Significant cardiovascular instability: *Chest compressions, vasoactive agent requirement, or multiple boluses of crystalloid or colloid.*
2) Symptomatic patent ductus arteriosus
3) Prolonged NPO status greater than 7 days

Feeding guidelines for preterm infants born less than 1500 g.

was more accurately obtained during chart review. Potential concomitant factors that could affect feeding tolerance were examined including treatment and/or prophylactic indomethacin use, dopamine requirement in first week of life, delivery room cardiopulmonary resuscitation, small for gestational age (SGA), and IUGR. Potential adverse outcomes including NEC, central line-associated bloodstream infection (as defined by CDC/NHSN), and death during NICU hospitalization were analyzed.[26]

Statistical analysis was performed using GraphPad Prism 6.0 (San Diego, California). Results are expressed as mean ± standard deviation. Data were compared using a *t* test or Mann-Whitney test, as appropriate. Statistical significance was considered at $P \leq .05$.

Our institution's Organizational Research Risk and Quality Improvement Review Panel approved the QI project, and the study was deemed exempt from the need for consent from institutional review board.

## RESULTS

A total of 95 infants with a birth weight of less than 1500 g (VLBW) were included in the analysis (Table 1; 59 infants in baseline [born in 2012-2013], and 36 in guidelines [born in 2014]). All infants were outborn and transferred to our NICU from a referring NICU. Six infants died (5 infants in the baseline group and 1 in the guidelines group) before 1 month of age; all were provided enteral feedings during their NICU hospitalization before death and were included in the analysis of feeding data, although all were omitted from growth velocity analysis at 1 month of age.

Overall demographic and clinical characteristics were similar between the 2 groups. The baseline group had a lower gestational age (27.3 ± 2.4 baseline vs 28.3 ± 2.7 guideline; $P < .05$), although there was no difference in mean birth weight compared with the guideline group. The numbers of infants with congenital anomalies were similar, and included infants with trisomy 21, sacrococcygeal teratoma, critical pulmonic stenosis, myelomeningocele with fetal repair, and trisomy 21 with myeloproliferative disorder.

Dopamine and prophylactic indomethacin use in the first week of life was significantly lower in the guideline group ($P < .05$; Table 1) than in the baseline group. Need for cardiopulmonary resuscitation in the delivery room was not different among the groups. SGA and IUGR infants were overrepresented in the guideline group ($P < .05$; Table 1). Human breast milk, either maternal or donor, was used for nearly all feeds in both groups.

Number of days NPO before initiation of enteral feeds decreased by 47% (4.83 ± 4.32 days baseline vs 2.58 ± 2.92 days guidelines; $P < .01$; Figure 2A). Total days on TPN decreased by 25% after the guidelines were established (16.29 ± 7.92 TPN days baseline vs 12.22 ± 6.92 days guidelines; $P < .01$; Figure 2B). Weight gain over the first month of life significantly increased after implementation of the

TABLE 1. Infant Characteristics and Outcomes

| | Baseline (n = 59) | Guidelines (n = 36) | *P* |
|---|---|---|---|
| Gestational age, wk, mean ± SD | 27.3 ± 2.4 | 28.3 ± 2.7[a] | .05 |
| Birth weight, g, mean ± SD | 1012 ± 275 | 1073 ± 278 | .30 |
| Infants with congenital anomalies, n (%) | 4 (7) | 2 (6) | .81 |
| Maternal or donor breast milk for first feed, n (%) | 56 (95) | 35 (97) | .59 |
| Prophylactic indomethacin, n (%) | 13 (22) | 1 (3)[a] | .01 |
| Treatment indomethacin, n (%) | 27 (46) | 10 (28) | .08 |
| Dopamine requirement in first week of life, n (%) | 30 (51) | 10 (28)[a] | .03 |
| CPR in delivery room, n (%) | 8 (14) | 3 (8) | .44 |
| Small for gestation age, n (%) | 5 (8) | 9 (25)[a] | .03 |
| Intrauterine growth restriction, n (%) | 3 (5) | 7 (19)[a] | .03 |
| Necrotizing enterocolitis, n (%) | 7 (12) | 3 (8) | .59 |
| Days of central line access, mean ± SD | 21.4 ± 18.4 | 21.8 ± 24.3 | .92 |
| Central line infection, n (%) | 2 (3) | 0 | .52 |
| Death before discharge, n (%) | 5 (8) | 1 (3) | .27 |

*Abbreviations: CPR, cardiopulmonary resuscitation; SD, standard deviation.*
[a]*Statistical significance (P < .05).*

VLBW feeding guidelines (14.45 ± 4.74 g/kg/d baseline vs 17.09 ± 6.15 g/kg/d guidelines; $P < .05$; Figure 2C).

Of the 6 patients with congenital anomalies, number of days NPO was 6.67 ± 4.23 and total days on TPN was 14.83 ± 5.98, which are not statistically different when comparing the group with anomalies to the whole cohort without anomalies. Two of these infants died before discharge.

Implementation of VLBW feeding guidelines did not impact the number of central line days, rates of NEC or central line-associated bloodstream infections, or mortality (Table 1).

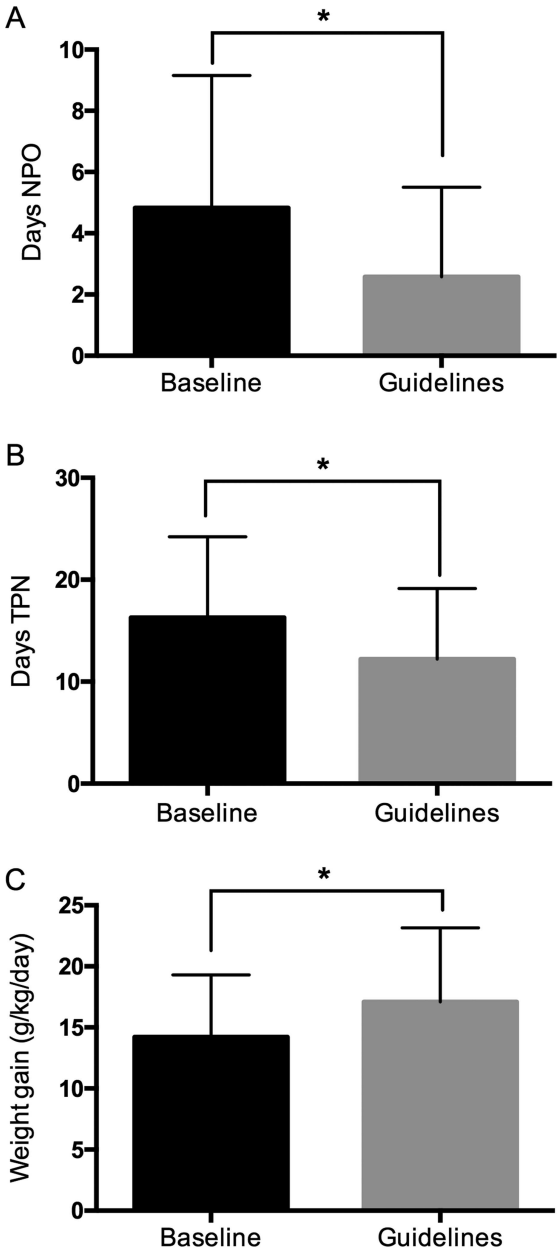
## DISCUSSION

The implementation of feeding guidelines in our NICU improved outcomes for VLBW infants. The aims of the project were to start enteral feeds sooner and to increase feeds faster, with the purpose of reducing the number of days on TPN and improving growth velocity at 1 month of age. During a 1-year time frame, we were able to demonstrate a significant improvement in our care of this fragile patient population.

The goal for nutrition and growth in premature infants is to mirror the growth of a fetus of the same gestational age.[10,27,28] This is often challenging clinically and remains an area of robust research, as postnatal growth failure can have long-term consequences including poor neurodevelopment.[28,29] Our QI project focused on the importance of enteral feeding of VLBW infants during their most clinically unstable time in the NICU, in order to improve growth velocity over the first month of life. By focusing on modifiable clinical feeding practices early in the hospital course of these infants, we were able to improve short-term outcomes. The effect of early feeding practices on long-term growth and developmental outcomes is uncertain, and demands further research.

Certain variables might have influenced our findings despite implementation of our guidelines. Baseline infants had a lower gestational age, a higher dopamine requirement, and were more likely to be treated with prophylactic indomethacin. This may indicate that this group was less clinically stable and had an increased risk for intestinal compromise. In contrast, the guideline infants were more likely to be IUGR or SGA, which are also a risk for feeding difficulties and the selected morbidities. Growth restriction, despite postnatal stability, has been associated with delay in feeding because of the increased risk of NEC.[18] These variables may have influenced the timing of initiation of enteral feeds as well as the rate of advancement. The data were also notable for a change in treatment practices for PDA, as fewer infants were given prophylactic or treatment doses of indomethacin in the later cohort, and in part due to the new guidelines our providers were more likely to allow trophic feedings while on indomethacin therapy. All of these factors may have influenced enteral feeding practices, but we demonstrated that the implementation of feeding guidelines ultimately resulted in earlier enteral feedings, shorter time on TPN, and improved growth without evidence of increased clinical morbidity.

FIGURE 2




Clinical outcomes after establishing feeding guidelines for VLBW infants. (A) Number of days NPO before start of enteral feeds. (B) Total days on TPN. (C) Weight gain over the first month of life. NPO indicates nil per os; TPN, total parenteral nutrition; VLBW, very low birth weight.

We anticipated that earlier achievement of full enteral feedings would also result in a reduction in central line utilization; however, we did not see a change in the number of central line days. Most preterm infants on TPN require central lines primarily to optimize nutrition, although other clinical conditions such as prolonged medication or antibiotic therapy may necessitate central venous access. During the period of this QI initiative, our NICU had active efforts in place to reduce central line infections, which included early removal of central lines and placement of peripheral intravenous line before achieving full enteral feedings. It is possible that those efforts had already influenced the length of time patients had a central line, so that no additional difference was seen with the feeding guideline intervention.

One of the potential limitations of this study was that adherence to the guidelines was not monitored on a daily basis. This could have been done by random review of medical records, but as stated previously, dedicated NICU dieticians were present on daily rounds to help encourage use of the guidelines. We felt that the education on feeding VLBW infants provided to the staff as well as reminders on rounds was the best way to implement the guidelines. Ultimately, the start and advancement of enteral feeds was up to the providing physician. This approach was felt to be best for the individual patients and the reproducibility for other units.

Because of the increased risk of feeding intolerance and complications, VLBW infants with major congenital anomalies are typically excluded from studies related to standardized feeding practices. Infants with complex congenital heart disease have a higher risk of poor intestinal perfusion and thus NEC, and infants with congenital anomalies have an increased risk of feeding complications.[28,30,31] Feeding guidelines for VLBW infants generally do not address this high-risk group, and these infants are typically fed with a conservative approach. We chose to include these infants to determine whether these infants would benefit from our guidelines without increasing morbidity. We found that VLBW infants with congenital anomalies in our NICU were fed more conservatively than VLBW infants without anomalies. Because of the limited number of infants with congenital malformations in this analysis, we are unable to make specific conclusions related to their tolerance and risk with enteral feedings. Further research into feeding practices for VLBW infants with major anomalies is needed.

Future interventions in our NICU could include addressing the frequency of feeds for VLBW infants. Studies have shown that feeds at 2-hour intervals are more tolerated than 3-hour intervals, thus allowing for these infants to reach full enteral feeds faster.[32,33] Another topic not addressed in our guidelines was when to initiate oral feeds, specifically breastfeeding. Traditionally, it is felt that infants are not physiologically capable of oral feeds before around 32 weeks corrected. There is current evidence that younger infants may tolerate breastfeeding as early as 27 to 28 weeks corrected, which could increase the number of infants breastfeeding at discharge.[34,35]

| Summary of Recommendations for Practice and Research | |
|---|---|
| **What we know:** | • The provision of adequate nutrition is a critically important facet of neonatal care.<br>• VLBW infants have unique developmental and clinical challenges that impair clinicians' ability to provide excellent nutrition.<br>• Standardization of feeding practices for preterm infants can improve growth and decrease secondary morbidities. |
| **What needs to be studied:** | • Optimal feeding strategies for VLBW infants must include evidence-based recommendations that address clinical risk factors for feeding intolerance.<br>• Rate of feeding advances in the setting of clinical factors such as vasopressor or indomethacin utilization, or fetal conditions or congenital anomalies that may impair intestinal blood flow.<br>• Strategies to implement best practices into clinical practice in the setting of complex intensive care in high-risk infants. |
| **What can we do today:** | • Develop team strategies to implement best practices in clinical care and foster a culture of improvement.<br>• Provide enteral nutrition to VLBW infants as early as clinically safe, in the form of minimal enteral nutrition or low-volume enteral feedings.<br>• Aim to reduce total parenteral nutrition and central line utilization.<br>• Standardize feeding practices and approaches to feeding intolerance to reduce the time to reach full enteral nutrition. |

Ultimately, the establishment of feeding guidelines in our NICU had a positive effect on short-term outcomes for our VLBW infants. Implementations of feeding guidelines such as those presented here are potentially generalizable to VLBW infants in other NICUs, and ultimately may improve growth and prevent secondary morbidities associated with prolonged TPN use.

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