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Transitioning Preterm Infants From Parenteral Nutrition: A Comparison of 2 Protocols

Malki Miller, MS, RD, CNSC^{1,2}, Keyur Donda, MBBS², Alok Bhutada, MD², Deepa Rastogi, MBBS, MS³, and Shantanu Rastogi, MD, MMM²

¹Department of Nutrition, Maimonides Infants and Children's Hospital, Brooklyn, New York, USA

²Division of Neonatology, Maimonides Infants and Children's Hospital, Brooklyn, New York, USA

³Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, New York, USA

Abstract

Background—Growth in preterm infants is compromised during the transition phase of nutrition, when parenteral nutrition (PN) volumes are weaned with advancing enteral nutrition (EN) feeds, likely due to suboptimal nutrient intakes during this time. We implemented new PN guidelines designed to maintain optimal nutrient intakes during the transition phase and compared growth outcomes of this cohort with a control group.

Materials and Methods—A chart review was conducted on infants born <32 weeks' gestation, before (control group) and after (study group) a new transition PN protocol was implemented in the neonatal intensive care unit. Weight parameters and nutrient intakes were calculated for the transition phase and compared between the 2 groups.

Results—Demographic and clinical characteristics of the 2 groups were comparable except for higher rates of sepsis in control group. Weight-for-age *z* scores at birth, at 1 week of life, and at the start of the transition phase were similar. At the end of the transition phase, infants in the study group had significantly higher *z* scores compared with the control group, even when corrected for sepsis, a difference that persisted at 35 weeks' gestation. During the transition phase, study infants gained 16.1 ± 4.6 g/kg/d compared with 13.2 ± 5.4 g/kg/d in control group ($P < .001$). Similar results were observed in the subset of expressed breastmilk-only fed infants (15.9 ± 4.6 g/kg/d in the study group compared with 13.2 ± 5.4 g/kg/d in the control group, $P < .004$).

Conclusion—Optimizing nutrition by the use of concentrated PN during the transition phase to maintain appropriate nutrient intakes improves growth rates in preterm infants.

Corresponding Author: Shantanu Rastogi, MD, MMM, Division of Neonatology, Maimonides Infants and Children's Hospital, 4802 Tenth Ave, F-119, Brooklyn, NY 11219, USA. srastogi@maimonidesmed.org.

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Statement of Authorship

M. Miller and S. Rastogi contributed to the conception and design of the study; contributed to acquisition, analysis, and interpretation of the data; and drafted the initial manuscript; K. Donda contributed to design of the study; contributed to acquisition, analysis, and interpretation of the data; and drafted the initial manuscript; A. Bhutada contributed to conception and design of the study; and D. Rastogi carried out the initial analyses and interpretation of the data. All authors critically revised the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Keywords

neonates; life cycle; enteral nutrition; parenteral nutrition; nutrition; outcomes research/quality; nutrition support practice

Clinical Relevancy Statement

Although established recommendations for optimal enteral and parenteral nutrient provision help to guide nutrition management of preterm infants in the neonatal intensive care unit, nutrient intakes during the transition period, when parenteral nutrition is weaned as enteral feeds are established, remain suboptimal and are associated with growth failure. Our study reports that a nutrition protocol specific to the transition phase results in improved growth rates in preterm infants.

Introduction

With increasing survival of preterm neonates, optimizing nutrition is emerging as an essential component in the medical management of this population. Although current nutrition recommendations aim to achieve postnatal growth rates approximating the intrauterine growth of a normal fetus of the same postmenstrual age,¹ we recently observed growth failure rates in our unit of close to 50%, with other studies reporting growth failure rates of 30%–97% among preterm infants.^{2–4} Poor nutrition is associated with adverse short-term outcomes, including sepsis, chronic lung disease, and prolonged need for mechanical ventilation, as well as impaired cognitive and neurological development in the long term.^{5–9} Therefore, maintaining adequate nutrition and growth in this high-risk population is an important goal in the neonatal intensive care unit (NICU).

Nutrition support of preterm infants begins immediately at birth, with early introduction of parenteral nutrition (PN). Trophic feeds are initiated as soon as possible, and as the infant matures physiologically, PN is slowly replaced with enteral nutrition (EN).^{10,11} Thus, the nutrition course of preterm neonates involves 3 phases: PN, the transition phase during which infants are weaned from PN as enteral feeds are established, and full EN. We previously showed the transition phase to be most vulnerable to inadequate nutrition, negatively affecting growth outcomes at discharge.⁴ Infants demonstrating growth inadequacy during this phase were 5 times more likely to be discharged with weights below the 10th percentile for corrected gestational age (CGA), with poor growth during this phase likely related to suboptimal energy and protein provision with a volume-based PN transition protocol. Our unit has since revised the PN guidelines to optimize nutrient provision throughout the duration of the transition phase, moving from our previous “volume-based” transition protocol to a “nutrient-based” transition protocol. Under the new protocol, nutrition management focuses on maintaining optimal energy and protein intakes throughout the transition phase, despite weaning PN. Our objective in this study was to assess the effectiveness of these revised nutrition practices during the transition phase in improving growth parameters at the end of the transition phase at 35 weeks’ CGA. We also proposed to elucidate the contribution of protein and energy intakes during the transition phase in the differences in growth outcomes.

Patients and Methods

Study Population

A chart review was conducted for a 2-year period prior to introduction of revised PN guidelines (June 2008–June 2010) for data on the control group and for 1 year (January–December 2012) after a change in transition PN guidelines was implemented in 2011. Infants included were those born less than 32 weeks' gestation with birth weights <2000 g, admitted to the NICU at Maimonides Infants and Children's Hospital during these study periods. Gestational age was estimated by obstetrical records obtained by early pregnancy ultrasound. Infants who were small for gestational age (birth weight below the 10th percentile when plotted on Fenton growth curves¹²), diagnosed with short bowel syndrome, transferred to another facility, or died during their NICU stay were excluded. Since our analysis included growth and nutrition parameters during the transition phase, we also excluded infants whose transition phase coincided with the use of steroids or furosemide, or a diagnosis of sepsis (determined by a positive blood or urine culture) or edema (determined by clinical examination and out-of-proportion weight gain with stable vital signs), since growth rates during this time would not accurately reflect nutrient provision. We also excluded infants whose transition phases started within the first week of life if they were still in the postbirth diuresis phase, since weight gain could not be accurately calculated (Figure 1). The study was approved by the Institutional Review Board at Maimonides Medical Center.

Nutrition Management

PN was initiated within 24 hours of birth, containing dextrose at a glucose infusion rate (GIR) of 4–6 mg/kg/min, amino acids (Trophamine; McGaw, Irvine, CA) at 2–3 g/kg/d, and lipids (Intralipid; Clintec, Deerfield, IL) at 0.5–1 g/kg/d. Calories were advanced daily based on metabolic tolerance, with a goal GIR of 11–14 mg/kg/min, amino acids of 3–4 g/kg/d, and lipids of 3 g/kg/d. Trophic feeds of expressed breastmilk (EBM) or preterm formula were initiated 24–72 hours postbirth, maintained at volumes <20 mL/kg/d for 3–10 days (based on gestational age), and thereafter advanced by 10–20 mL/kg/d to goal feeds of 160 mL/kg/d.

Transition PN Guidelines

Table 1 describes our guidelines for nutrition provision during the transition phase, defined as EN volumes of 20 mL/kg until full feeds (160 mL/kg). In the control group, the group that received a “volume-based” transition protocol, PN prescriptions were written as if the infant was nil per os (NPO), and the PN rate was adjusted to maintain a total fluid provision of 140 mL/kg/d. PN was discontinued when enteral feeds volumes of 100–120 mL/kg/d were reached, and powder human milk fortifier (Similac HMF; Abbott Nutritionals, Columbus, OH) was added to breastmilk. If no breastmilk was available, the infant received preterm infant formula of 20 kcal/oz, switched to 24 kcal/oz (Similac Special Care 24; Abbott Nutritionals, Columbus, OH) at EN volumes of 100–120 mL/kg/d.

In the study group, a “nutrition-based” transition protocol designed to maintain targeted kcal and protein intakes was implemented. When the infant reached EN feeds of 50 mL/kg/d, PN

nutrient prescriptions were concentrated in 100 mL/kg/d instead of the prescribed 140 mL/kg/d; consequently, each milliliter of PN provided approximately 40%–50% more dextrose and amino acids compared with our previous regimen. Parenteral dextrose, amino acid, and lipid prescriptions were adjusted daily to maintain a goal energy intake (combined feeds + PN) of 100–120 kcal/kg/d and protein intake of >3 g/kg/d, with parenteral lipids providing 50% of parenteral energy provision. Serum glucose and triglycerides were maintained within acceptable limits.

If the infant was fed breastmilk, powder human milk fortifier was added at EN volumes of 100–120 mL/kg/d, first at half-strength (22 kcal/oz) for 24 hours and then full strength (24 kcal/oz). If no breastmilk was available, preterm infant formula at 24 kcal/oz was used (Similac Special Care 24; Abbott Nutritionals) throughout the entire transition phase. PN was discontinued once the infant tolerated 100–120 mL/kg/d of enteral feeds.

Growth Outcomes

Body weights were measured 3 times weekly, on Mondays, Wednesdays, and Fridays. Growth rates (g/kg/d) and weight-for-age z scores at the start and end of the transition phase were calculated. Weight-for-age z scores at birth, after 1 week of life, and at 35 weeks' CGA were recorded. Growth velocity was calculated as grams per kilogram per day, by dividing the average daily weight gain (in grams) over the mean weight (in kilograms) during that time.

Calculation of Nutrition Intake

Energy and protein intakes and protein-energy ratios were calculated for all nutrition phases. For the PN phase, intakes were reported as an average of 3 days immediately prior to the transition phase, as a baseline comparison for intakes during the transition. PN nutrient intake during the transition phase was calculated at the volume-adjusted rate used to supplement enteral feeds to maintain prescribed total fluids, from enteral intakes of 30 mL/kg (when PN was likely to already be volume adjusted). For enteral feeds, EBM nutrient provision was estimated at 20 kcal/oz and 1.4 g protein/dL (accepted standards for preterm breastmilk nutrient composition¹³), and formula intakes were calculated based on kilocalories and protein composition of formula provided by manufacturers. To allow for a more accurate comparison of energy intakes between PN and EN, enteral caloric intakes were adjusted for predicted energy losses due to incomplete absorption and specific dynamic action, calculated at 85% of their original caloric value.¹⁴ Protein-energy ratios were calculated based on grams of protein provided per 100 kcal.

Clinical Factors

Clinical factors included in the analysis were those that are known to be associated with growth failure, such as broncho-pulmonary dysplasia (BPD) (need for supplemental oxygen at 36 weeks' CGA), sepsis (confirmed by a positive blood or urine culture), necrotizing enterocolitis (NEC) (presence of *Pneumatosis intestinalis*), and intraventricular hemorrhage (diagnosed by ultrasound and if grade 3).

Statistical Methods

The primary outcome of interest was the weight *z* score at the end of the transition phase and at 35 weeks' gestation, which was compared between the control and study groups. We also compared demographic, clinical, and nutrition factors between the 2 study groups to identify factors other than the intervention that may influence weight *z* score at the end of the transition phase and at 35 weeks. Continuous variables such as birth weight, gestational age, protein intake, and total calories were analyzed using the Student *t* test and reported as mean $\pm$ standard deviation (SD). Categorical variables, including sex, ethnicity, and incidence of clinical morbidities (eg, sepsis, NEC, and BPD) were compared between the groups using the χ^2 test or Fisher exact test (for variables with value <5 in any cell) and reported as proportion and percentage. Univariate linear regression analysis was conducted to elucidate the contribution of protein intake and nonprotein energy intake on growth velocity among the case and control groups as well as among the subset of breastmilk-fed babies.

We conducted multivariate linear regression analysis to identify the independent association of the demographic, clinical, and nutrition factors that were associated with weight *z* score at the end of the transition phase and at 35 weeks. To elucidate the influence of the updated PN guidelines on the exclusively breastmilk-fed infants, we conducted a similar analysis on a subset of the study group that was exclusively fed breastmilk during their stay in the NICU and compared them with the control group. Statistical analysis was done using STATA version 12 (StataCorp LP, College Station, TX). *P* values were set a priori at .05.

Results

Demographic and Clinical Characteristics of the Study Sample

The demographic and clinical characteristics of the study group ($n = 59$), the EBM-fed subset of the study group ($n = 41$), and control infants ($n = 134$) are summarized in Table 2. There were more males ($P < .03$) and lower rates of sepsis ($P < .02$) in the study group compared with the controls. Although the corrected gestational age of the study group at the start and end of the transition phase was lower compared with controls (start, 30.7 ± 0.4 weeks vs 31.4 ± 0.2 weeks, $P < .001$; end, 31.9 ± 0.4 wk vs 32.8 ± 0.2 wk, $P < .001$), the number of transition days did not differ (9.7 ± 3.5 days vs 10 ± 5.3 days, $P = .48$). Other demographic and clinical variables were similar between the groups. The difference in the proportion of males and rates of sepsis between the EBM-fed subset of the study group and controls did not reach statistical significance.

Comparison of Growth Velocity Between Study and Control Groups

Baseline weight-for-age *z* scores at birth, at 1 week of age, and at the start of the transition phase were comparable between groups, but the *z* scores at the end of the transition phase were significantly higher in the study group compared with the control group (-1.1 ± 0.5 vs -1.3 ± 0.5 ; $P < .01$); this observation was consistent with the higher growth velocity during the transition phase seen in the study vs control group (16 ± 4.6 g/kg/d vs 13.2 ± 5.4 g/kg/d; $P < .001$). This difference in weight-for-age *z* score persisted at 35 weeks' CGA (-1.5 ± 0.6 vs 1.2 ± 0.7 ; $P < .01$, Table 3). Given the difference in sex and prevalence of sepsis between study groups, we investigated their contribution to weight-for-age *z* score at the end of the

transition in the study group compared with the control group. While sepsis was associated with end-of-transition weight-for-age z score in both study ($\beta = -0.55$; 95% confidence interval [CI], -1.04 to -0.07 ; $P = .03$) and control groups ($\beta = -0.22$; 95% CI, -0.45 to -0.01 ; $P = .04$), there was no association of weight-for-age z score with sex. After adjusting for male sex and sepsis on multivariate regression analysis, weight-for-age z score at the end of the transition phase remained a significant predictor of z score at 35 weeks in the study group ($P < .001$; Table 4).

Because of the association between posttransition weight-for-age z scores and weight-for-age z score at 35 weeks, we examined the relationship between nutrient intakes during the transition phase and growth velocity. Energy, protein, and protein-energy ratios were higher overall in the study group compared with the control group (Figure 2, Tables 5 and 6). This difference was mainly accounted for by increases in parenteral energy and protein provision in concentrated PN formulations. Univariate linear regression analysis revealed that protein intake and nonprotein energy intake during the transition phase contributed to transition growth velocity for both study and control groups. However, the contribution of protein was higher in the study group vs controls (ie, protein intake explained 9% of the total growth velocity in the study group while it explained 4.5% of the growth velocity in the control group). Similarly, nonprotein energy intake explained 9.5% of the total growth velocity in the study group while it explained 5.3% of the total growth velocity.

Comparison of Growth Velocity Between EBM-Fed Infants in Study Group and Controls

We compared all controls with the EBM-fed subset of our study group. Demographic and clinical data were comparable between the groups (Table 2). There were no differences in weight-for-age z scores at any time point (Table 3). However, growth velocity during the transition phase remained significantly better in the EBM-fed subset of the study group vs controls (15.9 ± 4.6 g/kg/d vs 13.2 ± 5.4 g/kg/d, $P = .007$). Similar to our total study group, both protein and nonprotein energy intakes during the transition phase contributed to transition growth velocity for exclusively EBM-fed study and control groups. However, the contribution of protein was higher in the EBM-fed subset of the study group vs controls (ie, protein intake explained 20% of the total growth velocity in the EBM-fed subset of the study group while it explained 4.5% of the growth velocity in the control group). Similarly, nonprotein energy intake explained 18% of the total growth velocity in the EBM-fed subset of the study group while it explained 5.3% of the total growth velocity.

Discussion

In this study, we demonstrate improved nutrition provision, growth rates, and weight-for-age z scores among premature infants vulnerable to extrauterine growth failure, after the implementation of a nutrient-based protocol designed to maintain targeted energy and protein intakes throughout the duration of the transition phase of nutrition. We demonstrated improved growth velocity during the transition phase, resulting in higher weight-for-age z scores at the end of the transition phase among the study group that persisted until 35 weeks' CGA, and remained a significant predictor of weight-for-age z score at 35 weeks' CGA even

when corrected for other clinical factors. Higher weight-for-age *z* scores resulted from improvements in both protein and nonprotein energy intake during the transition phase.

As part of a multicenter study, our unit previously demonstrated extrauterine growth failure rates >30%.³ We also previously reported that the slowest extrauterine growth was during the transition phase, which predicted growth failure at discharge and was related to inadequate energy and protein intakes during this phase.⁴ To address this vulnerable period and promote continued growth, we established a nutrient-based transition protocol that resulted in significantly improved energy and protein intakes during the transition phase. The improvements in growth outcomes observed are consistent with previous studies that found better growth with increasing energy and protein intake throughout the NICU stay,^{15–18} although these improvements were not specifically associated with the critical period of extrauterine growth failure during the transition phase in these studies. While some studies implicate protein intake as the limiting nutrient factor for growth,¹⁹ we demonstrated growth failure during the transition phase to be related to both protein and energy, likely since both are compromised during this phase. Thus, improvement of both protein and non-protein energy is needed to prevent growth failure specific to the transition phase.

Since energy and protein intakes are more variable in EBM and thus adequate intakes to promote better growth are less assured compared with formula-fed infants,²⁰ we looked at the effects of our intervention specifically on growth outcomes of EBM-fed infants. Growth in this subset also improved, with better growth velocity during the transition phase mainly related to improved parenteral protein and nonprotein energy intakes. However, we did not observe differences in weight-for-age *z* scores at any time period. Several factors may have contributed to these findings. Other than the small sample size of the EBM-fed group, there was a bias in favor of the control group since growth rates in formula-fed infants are more ensured with fixed energy and protein intakes, and the control group comprised primarily formula-fed infants since historically, our rate of exclusive breastmilk use was low at ~12%. Thus, our improved growth outcomes in the EBM-fed subset are encouraging; indeed, the contribution of protein and energy to transition growth velocity was more pronounced overall in the breastmilk-fed only subset. This observation is promising in terms of its potential to decrease the incidence of extrauterine growth failure, as this intervention will better allow for the benefits associated with breastmilk use without compromising nutrient intakes during the transition phase, a problem likely to occur with the use of unfortified EBM during that time.

Our study highlights the importance of optimizing nutrition throughout the transition phase to maintain growth, avoiding energy and protein deficit associated with a lag in growth during a potentially critical window for neurological development,^{5–8} as well avoiding the need for future “catch-up” growth. There are emerging concerns regarding long-term adverse outcomes related to rapid weight gain during catch-up growth from growth-restricted preterm neonates. Metabolic syndrome has been reported in adulthood for term infants born small for gestational age,²¹ related to high insulin resistance and redistribution of body fat.^{21–23} Similarly, higher insulin resistance and increased intra-abdominal fat have been described among preterm infants at term gestational age compared with healthy term infants; one of the proposed reasons for these observations is rapid weight gain associated

with excessive energy given to promote catch-up growth after extrauterine growth failure.^{21,22} There is also emerging evidence of metabolic syndrome among children and young adults born preterm.²⁴ We therefore hypothesize that avoiding both growth failure during the transition period and its associated catch-up growth may potentially influence short-term neurological and long-term metabolic complications.

One of the limitations of our study is its retrospective design. While overall nutrition guidelines were comparable between the groups, evolving trends in neonatal nutrition management were reflected in our study. For example, the higher baseline protein intake observed in the study group reflected a more aggressive PN protein provision. Furthermore, trophic feeds were started earlier and advanced more quickly among the study group compared with controls, reflected in the lower CGA observed in the study group during the transition phase. Despite these differences, the weight *z* scores at the start of the transition phase were comparable between the 2 groups but were significantly different at the end of the transition phase, and growth velocity (in g/kg/d) was significantly higher in the study group; thus, changes in early nutrition practices likely did not confound our findings. Although differences in enteral intakes during the transition phase did reach statistical significance during some time points, this was related to the small variation in enteral energy value within control infants, and these energy differences were likely not clinically significant. We also did not include infants whose feeds advancement happened earlier, within the first week of life while they were still in the phase of early diuresis weight loss, as well as infants with clinically determined edema, although the numbers excluded were small (*n* = 4 in study group and *n* = 14 in control group). In addition, as we focused primarily on the transition phase, shown to be an important phase for infants with extra-uterine growth retardation, we did not track nutrient intakes until 35 weeks. It is possible that differences in nutrient intakes on full feeds, from the end of the transition phase until 35 weeks, may have accounted for weight gain; however, we do report similar nutrient intakes once the infant reached full EN (Tables 5 and 6).

Despite significant improvements in protein intake under our revised protocol, total protein intake still fell below the recommended 3.5 g/kg at some points during the transition phase, and thus further adjustment of our transition guidelines to reach recommended protein intake, in particular for the EBM-fed infants, may be warranted. While some units use a more customized approach to PN, daily adjusting PN fluid/ nutrient volume to complement enteral feeds intake, this practice is labor intensive, is prone to error and electrolyte abnormalities, and supplies a PN formulation that is inadequate in the event that the feeds are held (for feeds intolerance, sepsis, etc). Our transition protocol may be a more practical alternative for units looking to optimize nutrition provision, given the ease with which both protein and energy intakes were improved with sustained impact on weight gain at 35 weeks' CGA.

Conclusion

We demonstrate improved growth in preterm infants after implementing a protocol designed to optimize nutrition provision by concentrating PN during the transition phase. This transition PN protocol is a simple, practical, and effective method to address the nutrient

deficits inherent to the transition nutrition phase of preterm infants and may result in improved extrauterine growth.

References

1. Kleinman, R., editor. Pediatric Nutrition Handbook. 6. Elk Grove Village, IL: American Academy of Pediatrics; 2009. Nutritional needs of preterm infants; p. 79-112.
2. Clark RH, Thomas P, Peabody J. Extrauterine growth restriction remains a serious problem in prematurely born neonates. *Pediatrics*. 2003; 111(5):986–990. [PubMed: 12728076]
3. Stevens TP, Shields E, Campbell D, et al. Variation in enteral feeding practices and growth outcomes among very premature infants: a report from the New York State Perinatal Quality Collaborative. *Am J Perinatol*. 2016; 33:1–19. [PubMed: 26171600]
4. Miller M, Vaidya R, Rastogi D, Bhutata A, Rastogi S. From parenteral to enteral nutrition: a nutrition-based approach for evaluating postnatal growth failure in preterm infants. *JPEN J Parenter Enteral Nutr*. 2014; 38(4):489–497. [PubMed: 23674574]
5. Ehrenkranz RA, Dusick AM, Vohr BR, Wright LL, Wragge LA, Poole K. Growth in the neonatal intensive care unit influences neurodevelopmental and growth outcomes of extremely low birth weight infants. *Pediatrics*. 2006; 117(4):1253–1261. [PubMed: 16585322]
6. Lucas A, Morley R, Cole TJ. Randomized trial of early diet in preterm babies and later intelligence quotient. *BMJ*. 1998; 317:1481–1487. [PubMed: 9831573]
7. Hayakawa M, Okumura A, Hayakawa F, et al. Nutritional state and growth and functional maturation of the brain in extremely low birth weight infants. *Pediatrics*. 2003; 111(5):991–995. [PubMed: 12728078]
8. Tan MJ, Cooke RW. Improving head growth in very preterm infants: a randomized control trial I: neonatal outcomes. *Arch Dis Child Fetal Neonatal Ed*. 2008; 93:F337–F341. [PubMed: 18252814]
9. Ziegler EE, Carlson SJ. Early nutrition of very low birth weight infants. *J Matern Fetal Neonatal Med*. 2009; 22(3):191–197. [PubMed: 19330702]
10. Adamkin DH. Pragmatic approach to in-hospital nutrition in high-risk neonates. *J Perinatol*. 2005; 25:S7–S11. [PubMed: 15861175]
11. Rayyis SF, Ambalavanan N, Wright L, Carlo WA. Randomized trial of “slow” versus “fast” feed advancements on the incidence of necrotizing enterocolitis in very low birth weight infants. *Pediatrics*. 1999; 134(3):293–297.
12. Fenton TR. A new growth chart for preterm babies: Babson and Benda’s chart updated with recent data and a new format. *BMC Pediatr*. 2003; 3:13. [PubMed: 14678563]
13. Sapsford, AL. Composition of human milk and selected enteral products. In: Groh-Wargo, S. Thompson, M., Cox, JH., editors. *Nutritional Care for High-Risk Newborns*. 3. Chicago, IL: Precept Press; 2000.
14. Tsang, R., editor. *Nutrition of the Preterm Infant*. 2. Cincinnati, OH: Digital Educational Publishing; 2005. Energy; p. 27
15. Stoltz Sjöström E, Öhlund I, Ahlsson F, et al. Nutrient intakes independently affect growth in extremely preterm infants: results from a population-based study. *Acta Paediatr*. 2013; 102(11):1067–1074. [PubMed: 23855971]
16. Berry MA, Abrahamowicz M, Usher RH. Factors associated with growth of extremely premature infants during initial hospitalization. *Pediatrics*. 1997; 100(4):640–646. [PubMed: 9310518]
17. Ernst KD, Radmacher PG, Rafail ST, Adamkin DH. Postnatal malnutrition of extremely low birth-weight infants with catch-up growth postdischarge. *J Perinatol*. 2003; 23:477–482. [PubMed: 13679935]
18. Ziegler EE, Carlson SJ, Nelson SE. Interventional strategies to promote appropriate growth. *Nestle Nutr Inst Workshop Ser*. 2013; 74:181–192. [PubMed: 23887118]
19. Olsen IE, Richardson DK, Schmid CH, Ausman LM, Dwyer JT. Intersite differences in weight growth velocity of extremely premature infants. *Pediatrics*. 2002; 110(6):1125–1132. [PubMed: 12456909]

20. Prentice P, Ong KK, Schoemaker MH, et al. Breast milk nutrient content and infancy growth. *Acta Paediatr.* 2016; 105(6):641–647. [PubMed: 26865238]
21. Thureen PJ. The neonatologist's dilemma: catch-up growth or beneficial undernutrition in very low birth weight infants—what are optimal growth rates? *J Pediatr Gastro Nutr.* 2007; 45(suppl 3):S152–S154.
22. Uthaya S, Thomas EL, Hamilton G, Dore CJ, Bell J, Modi N. Altered adiposity after extremely preterm birth. *Pediatr Res.* 2005; 57(2):211–215. [PubMed: 15611357]
23. Hofman PL, Regan F, Cutfield WS. Prematurity—another example of perinatal metabolic programming? *Hormone Res.* 2006; 66:33–39. [PubMed: 16685134]
24. Lapillonne A, Griffin IJ. Feeding preterm infants today for later metabolic and cardiovascular outcomes. *J Pediatr.* 2013; 162:S7–S16. [PubMed: 23445851]

Figure 1.

Summary of inclusion of study and control population. SBS, short bowel syndrome; SGA, small for gestational age. *As detailed in the Patients and Methods section.

Figure 2.

(A) Energy intake during transition phase in study and control groups. $*P < .05$, total adjusted kilocalorie intake of study group vs controls. (B) Protein intake during transition phase in study and control groups. $*P < .05$, total protein intake of study group vs controls. (C) Protein-energy ratio during transition phase. $*P < .05$. EN, enteral nutrition; PN, parenteral nutrition.

Table 1

Summary of Parenteral Nutrition Guidelines Followed During Transition Phase in Study and Control Groups.

Transition Guidelines	Study Group	Control Group
Age at initiation of trophic feeds, d	1–2	1–2
EN volume at start of PN weaning, mL/kg	20	20
PN order during transition	At EN volumes of 50 mL/kg, full kcal and protein orders concentrated in 100 mL/kg; run at adjusted rate to maintain 140 mL/kg/d	Written for 140 mL/kg (as if infant is NPO); run at adjusted rate to maintain 140 mL/kg/d
EN volume at discontinuation of PN, mL/kg	80–120	80–120
Guidelines if feeds held	Run PN at full volume; add 5% dextrose solution at 40 mL/kg to maintain 140 mL/kg/d	Run PN at full volume (140 mL/kg)
Preferred feeds	Unfortified EBM	Unfortified EBM
EBM alternate	Preterm infant formula 24 kcal/oz	Preterm infant formula 20 kcal/oz

EBM, expressed breast milk; EN: enteral feeds; NPO, nil per os; PN, parenteral nutrition.

Table 2

Demographic and Clinical Characteristics of the Study Population.^a

Demographic/Clinical Characteristics	Study Group			P Value ^b	
	All (n = 59)	EBM Only (n = 41)	Controls (n = 134)	Study Group (All) vs Control	Study Group (EBM only) vs control
Ethnicity				.19	.26
White	21 (35.6)	14 (34.1)	39 (29.1)		
Asian	16 (27.1)	10 (24.4)	33 (24.6)		
Hispanic	18 (30.5)	12 (29.3)	43 (32.1)		
African American	7 (11.9)	4 (9.8)	18 (13.4)		
Other	1 (1.7)	1 (2.4)	16 (11.9)		
Males	43 (72.9)	28 (68)	77 (57.5)	.03	.06
Gestational age, mean $\pm$ SD, wk	29 $\pm$ 2.0	28.8 $\pm$ 2.2	28.9 $\pm$ 2.1	.46	.81
BW, mean $\pm$ SD, g	1331 $\pm$ 340	1292 $\pm$ 365	1283 $\pm$ 334	.26	.88
Postnatal steroids	2 (3.4)	2 (4.9)	4 (3.0)	.82	.61
IVH stage 3	0 (0)	0 (0)	8 (6.0)	.1	.21
BPD	5 (8.5)	3 (7.3)	11 (8.2)	.86	.98
Sepsis	4 (6.9)	3 (7.3)	28 (20.9)	.02	.1
NEC stage 2	2 (3.4)	1 (2.4)	10 (7.5)	.52	.46
Respiratory support on DOL 1					
Mechanical ventilation	14 (23.7)	11 (26.8)	39 (29.1)	.43	.93
CPAP	45 (76.3)	27 (65.9)	99 (73.9)	.39	.94
Room air	5 (8.5)	4 (9.8)	11 (8.2)	.78	.53

BPD, bronchopulmonary dysplasia; BW, birth weight; CPAP, continuous positive airway pressure; DOL, day of life; EBM, exclusive breastmilk; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis.

^aValues are presented as number (%) unless otherwise indicated.

^bP-value derived by *t* test for continuous variables and by χ^2 or Fisher exact test for categorical variables.

Table 3

Baseline Weight and Change in Weight z Score at Specific Time Points During the Neonatal Intensive Care Unit Stay.^a

Growth Parameters	Study Group			P Value ^b	
	All (n = 59)	EBM only (n = 41)	Controls (n = 134)	Study Group (All) vs Control	Study Group (EBM only) vs Control
z score at birth	-0.16 ± 0.6	-0.19 ± 0.6	-0.27 ± 0.5	.12	.38
z score at DOL 7	-0.97 ± 0.5	-1.01 ± 0.5	-1.02 ± 0.5	.40	.93
z score at start of transition	-1.02 ± 0.5	-1.1 ± 0.5	-1.1 ± 0.5	.25	.9
z score at end of transition	-1.1 ± 0.6	-1.2 ± 0.6	-1.3 ± 0.5	.008	.31
z score at CGA 35 weeks	-1.2 ± 0.7	-1.3 ± 0.7	-1.5 ± 0.6	.004	.22
Days to regain birth weight	12.1 ± 3.6	12.7 ± 3.9	12.2 ± 3.7	.69	.51
Growth velocity during transition, g/kg/d	16.1 ± 4.6	15.9 ± 4.6	13.2 ± 5.4	<.001	.007
Number of transition days	9.7 ± 3.5	10.2 ± 3.6	10 ± 5.3	.48	.81

CGA, corrected gestational age; DOL, day of life; EBM, exclusive breastmilk.

^aResults shown as mean ± SD.

^bP-value derived by *t* test.

Table 4Multivariate Regression Analysis of Factors Influencing Weight *z* Score at 35 Weeks.

Characteristic	β -Coefficient (95% Confidence Interval)	<i>P</i> Value
<i>z</i> Score at end of transition	0.99 (0.89 to 1.1)	<.001
Male sex	0.003 (−0.11 to 0.12)	.95
Sepsis	−0.15 (−0.29 to 0.001)	.06
Growth velocity during transition, g/kg/d	−0.002 (−0.02 to 0.02)	.85

Table 5

Enteral, Parenteral, and Total Adjusted Energy Intakes During Transition.

EN Volume, mL/kg	Energy Intake: EN, kcal/kg/d		Energy Intake: PN, kcal/kg/d		Total Energy Intake: EN + PN, kcal/kg/d	
	Study Group (n = 59)	Controls (n = 134)	Study Group (n = 59)	Controls (n = 134)	Study Group (n = 59)	Controls (n = 134)
0	0 ± 0	0 ± 0	86.5 ^a ± 13.8	92.0 ± 12.5	86.5 ^a ± 13.8	92.0 ± 12.5
30	17.9 ^a ± 1.4	17.0 ± 0	78.7 ± 7.9	80.3 ± 6.9	96.6 ± 8.1	97.3 ± 8.9
40	23.9 ^a ± 1.9	22.7 ± 0	74.5 ± 6.5	75.4 ± 5.4	98.4 ± 6.8	98.1 ± 8.1
50	29.9 ^a ± 2.4	28.3 ± 0	73.6 ^a ± 9.2	70.3 ± 4.8	103.5 ^a ± 9.3	98.7 ± 4.8
60	36.0 ^a ± 2.9	34.0 ± 0	69.2 ^a ± 8.8	64.8 ± 4.4	105.2 ^a ± 8.9	98.8 ± 4.4
70	42.1 ^a ± 3.4	39.7 ± 0.6	63.5 ^a ± 8.2	59.1 ± 3.9	105.5 ^a ± 8.3	98.8 ± 4.0
80	48.0 ^a ± 3.9	45.9 ± 2.3	55.8 ^a ± 7.6	52.4 ± 6.2	103.8 ^a ± 7.7	98.3 ± 8.0
90	54.3 ^a ± 4.5	52.2 ± 3.3	47.6 ^a ± 7.2	41.0 ± 16.1	101.9 ^a ± 9.9	93.2 ± 16.1
100	61.8 ^a ± 4.9	60.1 ± 5.2	35.4 ^a ± 7.5	26.2 ± 20.1	97.2 ^a ± 15.7	86.3 ± 19.7
110	69.4 ± 5.7	67.6 ± 6.2	19.3 ^a ± 6.7	13.6 ± 17.7	88.6 ^a ± 16.8	81.2 ± 17.8
120	77.6 ^a ± 5.4	73.9 ± 6.8	8.5 ± 14.2	6.4 ± 13.9	86.2 ^a ± 13.2	80.4 ± 14.4
130	85.3 ± 5.3	84.8 ± 6.4	0 ± 0	0 ± 0	86.9 ± 6.6	86.4 ± 9.2
140	92.8 ± 5.1	92.6 ± 5.9	0 ± 0	0 ± 0	93.6 ± 5.7	92.6 ± 5.9
150	100.4 ± 4.4	99.6 ± 5.9	0 ± 0	0 ± 0	101.5 ± 7.5	99.6 ± 5.9
160	108.5 ± 1.4	107.8 ± 4.1	0 ± 0	0 ± 0	108.5 ± 1.4	107.9 ± 4.1

EN, enteral nutrition; PN, parenteral nutrition.

^a $P < .05$ vs controls.

Table 6

Enteral, Parenteral, and Total Protein Intakes During Transition.

EN Volume, mL/kg	Protein Intake: EN, g/kg/d		Protein Intake: PN, g/kg/d		Total Protein Intake: EN + PN, g/kg/d	
	Study Group (n = 59)	Controls (n = 134)	Study Group (n = 59)	Controls (n = 134)	Study Group (n = 59)	Controls (n = 134)
0	0 ± 0	0 ± 0	3.3 ^a ± 0.4	3.1 ± 0.3	3.3 ^a ± 0.4	3.1 ± 0.3
30	0.5 ± 0.1	0.5 ± 0.1	2.6 ^a ± 0.3	2.5 ± 0.2	3.1 ^a ± 0.4	2.9 ± 0.2
40	0.7 ^a ± 0.2	0.6 ± 0.1	2.4 ^a ± 0.3	2.2 ± 0.2	3.0 ^a ± 0.4	2.8 ± 0.3
50	0.9 ^a ± 0.2	0.8 ± 0.1	2.4 ^a ± 0.5	2.0 ± 0.2	3.2 ^a ± 0.6	2.7 ± 0.2
60	1.0 ^a ± 0.3	0.9 ± 0.1	2.3 ^a ± 0.5	1.7 ± 0.2	3.3 ^a ± 0.6	2.6 ± 0.2
70	1.2 ^a ± 0.3	1.1 ± 0.1	2.3 ^a ± 0.4	1.5 ± 0.2	3.5 ^a ± 0.5	2.5 ± 0.2
80	1.4 ^a ± 0.3	1.3 ± 0.2	1.9 ^a ± 0.3	1.2 ± 0.2	3.3 ^a ± 0.5	2.5 ± 0.3
90	1.6 ± 0.4	1.5 ± 0.3	1.6 ^a ± 0.2	0.9 ± 0.3	3.1 ^a ± 0.5	2.3 ± 0.4
100	1.9 ± 0.4	1.8 ± 0.4	1.1 ^a ± 0.2	0.5 ± 0.4	3.0 ^a ± 0.6	2.3 ± 0.5
110	2.2 ± 0.5	2.1 ± 0.5	0.5 ^a ± 0.3	0.2 ± 0.3	2.7 ^a ± 0.6	2.3 ± 0.5
120	2.5 ± 0.5	2.5 ± 0.5	0.2 ^a ± 0.3	0.1 ± 0.1	2.7 ± 0.5	2.6 ± 0.5
130	2.8 ± 0.5	2.9 ± 0.5	0 ± 0	0 ± 0	2.8 ± 0.5	2.9 ± 0.5
140	3.1 ± 0.4	3.2 ± 0.4	0 ± 0	0 ± 0	3.1 ± 0.4	3.2 ± 0.4
150	3.5 ± 0.4	3.4 ± 0.4	0 ± 0	0 ± 0	3.5 ± 0.4	3.4 ± 0.4
160	3.8 ± 0.1	3.8 ± 0.3	0 ± 0	0 ± 0	3.8 ± 0.1	3.8 ± 0.3

EN, enteral nutrition; PN, parenteral nutrition.

^a $P < .05$ vs controls.