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Very low birth weight infant care: adherence to a new nutrition protocol improves growth outcomes and reduces infectious risk

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ABSTRACT

Background: Very low birth weight (VLBW) infants are at risk for postnatal growth restriction due to inadequate nutrient delivery and concomitant illness. Integrated clinical pathways or protocols can improve growth outcomes by decreasing practice variability.
Methods: A comprehensive nutrition bundle comprising standardized recommendations for initiating, advancing, and fortifying enteral feedings, and timely discontinuation of central lines was implemented in July 2012. Eligible were infants with a birth weight of <1500 g and <34 weeks gestation who were born over a 1-year period pre- and post-intervention, respectively. The primary aim was to determine if the intervention improved anthropometric parameter delta *z* scores at 36 weeks PMA. Secondary aims included time to first and full enteral feedings, central line-days, and rates of necrotizing enterocolitis (NEC) and sepsis/sepsis-like episodes.
Results: A total of 299 infants were included, of which 156 received the proposed intervention (Nutrition bundle group), and 143 received non-standardized nutrition practices (Conventional group). Median delta *z* scores for length (−1.2 versus −1.71; $p = 0.01$) and head circumference (−0.73 versus −1.21; $p = 0.03$) but not weight at 36 weeks PMA (−1.42 versus −1.58; $p = 0.74$) were significantly higher in the Nutrition bundle group as compared to the Conventional group. Fewer infants in the intervention group had severe growth restriction. Time to first feed, full feeds, and central line duration were significantly shorter in the intervention period. The incidence of NEC and sepsis/sepsis-like episodes decreased with the intervention.
Conclusions: A strategy using a comprehensive nutrition bundle improved linear and head circumference growth, reduced postnatal growth restriction, and decreased comorbidities in VLBW infants.

1. Introduction

Very low birth weight (VLBW) infants with inadequate postnatal growth experience comorbidities of prematurity (e.g., chronic lung disease, postnatal infection) [1] and neurodevelopmental impairments more frequently when compared to those with adequate growth [2]. Poor growth following premature birth may also play a role in the development of chronic adult diseases such as hypertension, diabetes, obesity, and hyperlipidemia [3–5]. However, optimal postnatal growth goals for preterm infants, which ideally would mirror the fetal growth at a comparable gestational age, are often difficult to achieve [6]. For this reason, nutrient deficits are common, very difficult to replenish, and especially pronounced when birth occurs before 31 weeks gestation [7]. Cumulative deficiencies in protein and energy limited just to the first week of life can lead not only to subsequent postnatal growth restriction but also poorer neurodevelopmental outcomes at 18 months [8]. Longer nutritional deficits involving weight gain from birth to hospital discharge can impact motor development in early childhood [9], while both early neonatal weight gain and post-discharge head growth can influence long-term cognitive outcome [10].

Despite accumulating research, increased knowledge, and product improvement, optimal management of nutrition in preterm infants in the neonatal intensive care unit (NICU) remains a challenge, as evidence-based interventions are often not applied uniformly to daily practice. An approach shown to reduce medical practice variation, enhance quality of care, contain costs, and improve outcomes is the development of integrated clinical pathways or clinical protocols [11,12]. Troche *et al.* demonstrated that the incidence of NEC was

Abbreviations: CLD, chronic lung disease; NEC, necrotizing enterocolitis; PMA, postmenstrual age; VLBW, very low birth weight.

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significantly reduced by the introduction of a standardized feeding protocol in a large cohort of critically ill infants weighing 1250 to 2500 g at birth [13]. More recent studies have demonstrated that implementing standardized feeding protocols can also improve growth outcomes, in addition to reducing adverse events [11,14].

At our institution, a one-year retrospective review of nutritional practices for preterm infants in 2012 revealed substantial provider variability and nutrition-related comorbidities. As a result, a comprehensive standardized nutrition protocol for preterm infants was created in order to reduce heterogeneous practices and improve nutrition-related outcomes. It included several key changes in practice that were shown in the literature to improve postnatal growth [15] and decrease infectious risk [16]. These included early initiation of enteral feedings, earlier fortification of breast milk feedings, standard advancement of enteral feedings based on gestational age, increased protein delivery, and early discontinuation of central lines.

This study was designed to determine the impact of the standardized Nutrition bundle protocol on postnatal growth at discharge. We hypothesized change in practice would result in improved growth parameters at 36 weeks postmenstrual age (PMA) and a significant decrease in the percentage of VLBW infants with postnatal growth restriction. The primary objectives of the study were to determine if the nutritional bundle intervention improved weight gain, linear and head circumference growth at 36 weeks PMA, and decreased proportion of infants who were severely (less than 3 SD or 3rd percentile) or moderately (less than 2 SD or 10th percentile) restricted for weight, head circumference and length, respectively, at discharge. The secondary objectives were to assess the effects of intervention on times to first and full enteral feedings, central line-days and rates of necrotizing enterocolitis (NEC), and sepsis/sepsis-like episodes.

2. Methods

2.1. Population, location, and intervention

This study took place at the Monroe Carell Jr. Children's Hospital NICU at Vanderbilt University in Nashville, Tennessee. Our level IV unit receives nearly 1500 admissions yearly, including approximately 200 VLBW infants. In July 2012, a multi-disciplinary team composed of dietitians, neonatologists, lactation consultants, nurses, and a pharmacist developed a comprehensive, standardized Nutrition bundle protocol containing potentially better practices after critical appraisal of existing literature (Supplemental Fig. 1; Preterm Infant Nutrition Quick Reference). The protocol aimed to standardize and bundle nutrition practices in four areas**:** (1) initiation, advancement, and weaning of parenteral nutrition; (2) early initiation of enteral feedings and standard advancement; (3) use of standard fortification recipes of breast milk with a targeted nutrient goal as recommended by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition [17]; and (4) earlier discontinuation of central lines used for parenteral nutrition.

The protocol includes absolute and relative contraindications to enteral feedings, with a strong recommendation for enteral feedings to commence within 24 h of birth. Feeding advancement was stratified by gestational age, and the goal caloric intake was 120 kcal/kg/day. Infants received donor breastmilk, by informed maternal consent, if maternal breastmilk was unavailable. Transition from donor breastmilk to preterm formula was made at 34 weeks PMA if maternal breastmilk was unavailable. Prior to the intervention, preterm formula was given in instances when maternal breast milk was not available. Both study groups received standard parenteral nutrition with 2.5–3 g/kg protein on the day of birth. Protein content of the custom parenteral nutrition was increased over 2 to 4 days up to 3.5 g/kg/day in the Conventional and 4 g/kg/day in the Nutrition bundle group. The protocol recommended that both parenteral nutrition and central lines be discontinued when enteral feedings reach a volume of 100–120 ml/kg/day. Enteral protein goals were 3.5–4 g/kg/day in the Conventional group and 4–4.5 g/kg/day during the intervention, with patients born <1250 g receiving the higher end of the recommended protein range. The nutrition bundle continued until patient discharge from the NICU.

All infants born at less than 34 weeks gestation and less than 1500 g were eligible for the study. Infants born between July 1, 2011 and June 30, 2012 comprised the Conventional group and those born between July 1, 2012 and June 30, 2013 composed the Nutrition bundle (intervention) group. Infants with major chromosomal or genetic anomalies and structural gastrointestinal defects at birth as well as infants who were transferred to our facility after 48 h of life were excluded. Information on baseline infant characteristics, including gestational age, birth weight, length, head circumference, gender, mode of delivery, Apgar score at 5 min of life, CRIB score (a measure of illness in the first 24 h of life) [18], and use of antenatal steroids were extracted from electronic medical records for the Conventional group and prospectively collected for the Nutrition bundle group. At our institution, all feeding and parenteral nutrition orders, physician notes, anthropometric data, feeding type, and volume are solely entered in the electronic medical record, allowing for complete data set extraction. Total actual protein delivery was not calculated by the electronic medical record and therefore was only calculated in random audits. Daily weights were obtained without clothes and diaper on calibrated scales and recorded to the nearest 5 g.

Weekly head circumference and length were measured using a paper unstretchable tape and rounded to the nearest millimeter, as per unit standard.

2.2. Quality metrics

Three quality measure tools were used to quantify study processes and outcomes, protocol compliance, and primary and secondary outcomes. The following items were monitored for compliance with the protocol using random audits: attainment of goal protein and lipid at 7 days of life, initiation of enteral feedings in the first 2 days of life, advancement of enteral feedings according to protocol, time to reach full enteral feedings, and time to fortification of human breastmilk. The audits were performed by a team of dietitians and nurse practitioners trained in quality improvement strategies who were part of the multi-disciplinary quality improvement nutrition team. Data was collected on breastmilk usage at discharge due to concerns that use of donor breastmilk might discourage mothers from providing their own breastmilk. During the study, medical providers and staff were updated on bundle compliance every 3 months.

Outcome quality measures were used to assess primary outcomes. The primary outcomes of the study were growth indices at 36 weeks PMA and the incidence of moderate and severe postnatal growth restriction at discharge. We chose to compare the study infants at 36 weeks PMA in order to eliminate the variability created by different lengths of stay for each infant. Moderate and severe postnatal growth restriction were defined as (1) weight *z* score at discharge below 2 and 3 SD, respectively; (2) length *z* score at discharge for 2 and 3 SD, respectively; and (3) head circumference *z* score at discharge for 2 and 3 SD, respectively.

Balancing measures were used to measure secondary outcomes. Data on central line days, rates of NEC, and sepsis were extracted from electronic medical records. As per our unit's standard of care, the proceduralist is required to complete a procedural note containing the date and time of each insertion and each discontinuation of a central line for each infant. NEC was defined as Bell stage 2 or higher as per the modified Bell's classification or when diagnosed at surgery. Sepsis was defined as blood culture-positive or culture-negative sepsis-like episode which was treated for at least 5 days with antibiotics. We also collected data on other common comorbidities such as chronic lung disease (CLD), severe intraventricular hemorrhage (grades 3 and 4), periventricular leukomalacia, retinopathy of prematurity, patent ductus