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Oral feeding practices and discharge timing for moderately preterm infants☆

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ABSTRACT

Background: Oral feeding skills of moderately preterm infants are not mature at birth.
Aims: To establish the relationship between postmenstrual age at introduction of first oral feeding and attainment of full oral feeding and hospital discharge for moderately preterm infants.
Study design: Multicenter retrospective analysis of a prospective cohort of moderately preterm infants admitted to a *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Neonatal Research Network hospital.
Subjects: 6146 infants born at 29–33 weeks' gestation from January 2012 to November 2013.
Outcome measures: Postmenstrual age at full oral feeding and at hospital discharge.
Results: The median postmenstrual age at first oral feeding was 33.9 weeks (interquartile range 33.1–34.3). For each week earlier at first oral feeding, full oral feeding occurred 4.5 days earlier ($p < 0.0001$) and hospital stay was shortened by 3.4 days ($p < 0.0001$). Higher birth weight ($p < 0.0001$) and black maternal race ($p = 0.0001$) were associated with younger postmenstrual age at full oral feeding and at discharge.
Conclusion: Moderately preterm infants with earlier introduction of oral feeding achieved earlier full oral feeding and hospital discharge.

1. Introduction

In 2015, approximately 83,000 out of 383,000 preterm infants born in the U.S. were born between 28 and 33 weeks' gestation [1]. Given the number of infants born in this gestational age range, care of the moderately preterm (MPT) population accounts for significant resource use in the neonatal period, and evidence-based care practices to guide their care should be sought. Scandinavian population-based studies provide insight into the financial impact of prematurity and its associated morbidities [2,3]. In a Norwegian cohort, 1 in 12 adults born at 28–30 weeks and 1 in 24 adults born at 31–33 weeks received disability pension compared with 1 in 59 term-born adults [2]. Similarly, a Swedish cohort of adults born at 29–32 weeks showed a 70.1% employment rate and 5.6% disability rate compared with 74.1% employment and 1.5% disability for term-born adults [3]. Optimizing nutrition for infants in this gestational age range has the potential to enhance neurodevelopmental outcomes.

The importance of establishing early nutrition is increasingly recognized, especially among the extremely preterm and growth-restricted populations. The nutritional demands of MPT infants have not received the same attention, although a call for awareness of the feeding issues in this population has been made [4]. A body of evidence to guide practice for the MPT infant is lacking, and frequently the enteral nutrition of MPTs is managed in a similar manner as it is for extremely preterm infants. Beyond the timing of introduction and advancement of enteral feeding, oral feeding is a focus for the MPT population, as feeding-related difficulties are an often-cited reason for hospitalization beyond 36 weeks postmenstrual age (PMA). Oral feeding skills develop through the course of a full-term gestation with the emergence of coordinated sucking and swallowing at 32–34 weeks

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[5]. Even in the absence of respiratory disease, MPT infants typically have immature coordination of sucking and swallowing. Maturation of feeding behaviors, including sucking and swallowing, continues from 33 to 36 weeks PMA [6].

Feeding protocols based on infant cues place the infant in control of the frequency and quantity of oral intake. Non-nutritive sucking and cue-based feeding beginning as early as 32 weeks PMA have been shown to shorten the length of hospital stay [7,8]. Discharge criteria for newborns in the NICU include a consistent oral feeding pattern to support weight gain without compromising respiratory status. The impact of feeding practices on length of stay in the MPT population merits exploration. We hypothesized that MPT infants whose first oral feeding occurred at an earlier PMA would achieve full oral feeding sooner than those for whom oral feeding was introduced at a later PMA. Our secondary hypotheses were that MPT infants whose first oral feeding occurred at an earlier PMA would have a shorter length of hospitalization and would be less likely to remain hospitalized at 36 weeks PMA due to inadequate oral feeding.

2. Material and methods

2.1. Subjects

This was a retrospective analysis of a prospective cohort of MPT infants, defined as those born at 29 through 33 weeks' gestation, admitted to a *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Neonatal Research Network hospital within 72 h of birth. The cohort has been previously described in comparison to more preterm infants [9]. Gestational age was determined by obstetrical best estimate based on last menstrual period, obstetrical parameters, and/or early prenatal ultrasound. If obstetrical estimate was not available, then the neonatologist's estimate based on physical, neurological, and/or lens examination was used to determine gestational age. The gestational age range was selected to be in continuity with the more preterm infants evaluated by the NICHD Neonatal Research Network. The study period lasted 22 months from January 2012 through November 2013. Exclusion criteria included a prenatal decision to withdraw or limit intensive care, congenital anomalies, birth weight < 750 g (to limit the inclusion of severely growth restricted infants), unknown date of first oral feeding, and death before achievement of full oral feeding.

2.2. Measurements

Data were collected prospectively by trained research coordinators and included maternal and neonatal characteristics, treatments, morbidities, and mortality. The institutional review board at each center approved the registry. The primary outcome for the analysis was the PMA at which full oral feeding was achieved. Full oral feeding was defined for this study as intake of 120 ml/kg/d. Secondary outcomes included PMA at hospital discharge and inadequate oral feeding as the primary indication for ongoing hospitalization at 36 weeks PMA. Research coordinators reviewed the medical record to determine the primary reason an infant remained hospitalized at 36 weeks PMA (respiratory, apnea/bradycardia, inadequate oral feeding, or other indication). If multiple problems documented, the research coordinator consulted with the NRN center principal investigator to determine the primary reason for ongoing hospitalization at 36 weeks PMA.

2.3. Data analysis

Median regression was performed to examine relationships of continuous outcomes, such as PMA at full oral feeding and PMA at hospital discharge, to age at first oral feeding, and logistic regression analysis was used to examine such relationships for categorical outcomes. Median regression is robust to outliers and skewed distributions. Median regression estimates the conditional median of the response variable given certain values of the predictor variables or covariates, rather than estimating the conditional mean as in the case of least square methods. All models were adjusted for birth weight, small for gestational age (SGA) status, sex, multiple births, maternal race, surfactant exposure, treatment of patent ductus arteriosus (PDA), human milk exposure (maternal and/or donor), and center. Because feeding protocols were not standardized across the Network, center was included in all adjusted analyses. These variables were selected a priori as covariates for the model due to plausible relationships to the primary outcome. Adjusted median differences are reported for the continuous outcomes. Odds ratios and 95% confidence intervals (95% CIs) are reported for the categorical outcomes. Statistical significance was set at 0.05 and was, in general, associated with 95% CIs that did not cross 0 for continuous variables and 1 for categorical variables (odds ratios).

3. Results

There were 7057 infants enrolled in the Moderate Preterm Registry; 6146 remained after exclusion for congenital anomalies (n = 624), prenatal decision to withdraw or limit intensive care (n = 2), birth weight < 750 g (n = 43), unknown date of first oral feeding (n = 230), death prior to achievement of full oral feeding (n = 9), or missing exclusion criteria data (n = 3) (Fig. 1).

3.1. Relationship of PMA at first oral feed to PMA at full oral feeding

Infants whose first oral feeding occurred before 33 weeks PMA had younger gestational age at birth than those whose first oral feeding occurred at or after 33 weeks PMA ($p < 0.0001$, Table 1). Median regression analysis confirmed the highly significant association of PMA at first oral feeding with PMA at full oral feeding (Table 2). The median PMA at first oral feeding was 33.9 weeks (IQR 33.1–34.3). For each week earlier in PMA at first oral feeding, full oral feeding occurred 4.5 days sooner (95% CI 4.1–4.8, $p < 0.0001$). Higher birth weight ($p < 0.0001$), black maternal race ($p = 0.0001$), and singleton status ($p = 0.021$) were associated with younger PMA at full oral feeding. For every 100 g increase in birth weight, the PMA at full oral feeding decreased by 0.5 days (95% CI 0.4–0.5, $p < 0.0001$). Black infants achieved full oral feeding 1.6 days earlier than infants of other races (95% CI 0.8–2.4, $p = 0.0001$). Singletons achieved full oral feeding 0.6 day earlier than infants who were part of multiple births (95%CI 0.1–1.0, $p = 0.021$). Factors associated with older PMA at full oral feeding included male sex ($p < 0.0001$), SGA status ($p = 0.008$), surfactant exposure ($p < 0.0001$), PDA requiring treatment ($p = 0.007$), and human milk exposure ($p = 0.022$). Male infants achieved full oral feeding 1.3 days later than females (95% CI 0.9–1.8, $p < 0.0001$). Those infants born SGA reached full oral feeding 0.9 days later than other infants (95% CI 0.2–1.6, $p = 0.008$). Infants exposed to surfactant achieved full oral feeding 1.8 days later than infants who did not receive surfactant (95% CI 0.1–1.1, $p = 0.021$). The infants who underwent pharmacologic or surgical treatment of a PDA achieved full oral feeding 3.4 days later than infants who did not receive treatment (95% CI 0.9–5.8, $p = 0.007$). Infants exposed to any human milk in the first 28 days of life achieved full oral feeding 0.8 days later than infants who had no human milk exposure in the first 28 days (95% CI 0.1–1.4, $p = 0.023$). Human milk exposure in the first 28 days varied by gestational age with the highest incidence in the infants born at 29 weeks' gestation (91.9%) and the lowest incidence at 33 weeks' gestation (82.2%, Table 3).

3.2. Relationship of PMA at first oral feeding to PMA at hospital discharge

We analyzed the impact of the timing of introduction of oral feeding on the length of hospital stay. For each week earlier in PMA at first oral feeding, discharge occurred 3.4 days earlier when measured by PMA