Effects of Donor Breastmilk Feeding on Growth and Early Neurodevelopmental Outcomes in Preterm Infants: An Observational Study

Laura S. Madore, MD[1,2,†]; Samudragupta Bora, PhD[3,‡]; Carmina Erdei, MD[1,3]; Tina Jumani, DO[1,¶]; Allison R. Dengos, DO[1,¥]; and Sarbattama Sen, MD[1,3]

[1]Department of Pediatric Newborn Medicine, Tufts Medical Center, Boston, Massachusetts; [2]Department of Pediatric Newborn Medicine, Baystate Medical Center, Springfield, Massachusetts; and [3]Department of Pediatric Newborn Medicine, Brigham and Women's Hospital, Boston, Massachusetts

ABSTRACT

Purpose: Donor breastmilk (DBM) has gained popularity as an alternative to formula when mother's own milk (MOM) is unavailable. The objective of this study was to evaluate the effects of a predominantly DBM diet on growth and subsequent neurodevelopment in preterm infants at a level 3 neonatal intensive care unit (NICU).

Methods: This single-center, observational cohort study compared data from preterm infants supplemented with predominantly (>50%) DBM to those from age- and weight-matched infants fed only MOM or supplemented with predominantly (>50%) preterm formula (PF). The primary outcome was in-hospital weight gain, and the secondary outcome was neurodevelopment, as assessed by the Bayley III scale at 1 and 2 years' corrected age. Exclusion criteria were major congenital defects, death prior to discharge from the NICU, or supplementation volumes of <50% over the first month of life. We compared the outcomes among the 3 feeding groups with the χ^2 test, ANOVA, and ANCOVA, with post hoc pairwise comparisons after adjustment for the following confounders: bronchopulmonary dysplasia, multiple births, and social work involvement.

Findings: In the entire cohort, the mean gestational age was 27.1 weeks and the mean birthweight was 914 g. The DBM (n = 27) and PF (n = 25) groups were similar with regard to socioeconomic characteristics. DBM infants regained birthweight more slowly over the first month of life compared with infants fed MOM (n = 29) or PF (mean [SD], 17.9 [5.7], 22.0 [6.8], and 20.3 [5.7] g/kg/d, respectively; $P = 0.05$); however, this growth difference was attenuated at later time points. In a fully adjusted model, the DBM group scored significantly lower in cognition at both 1 year ($P = 0.005$) and 2 years ($P = 0.03$) of age compared with the infants fed non-DBM diets.

Implications: The findings from this study suggest that in this NICU, preterm infants supplemented with predominantly DBM had compromised early in-hospital weight gain and, possibly, early cognitive delays compared with infants fed only MOM or infants supplemented with predominantly PF. These findings reinforce the need for further research on the optimal use of DBM in the preterm population and a continued need for promoting breastfeeding efforts to supply MOM. (*Clin Ther*. 2017;39:1210–1220)

Key words: donor breastmilk, growth, neurodevelopment, preterm infants.

INTRODUCTION

Mother's own milk (MOM) is the optimal form of nutrition in all infants, particularly the vulnerable preterm population.[1] Compared with formula feeding, breastmilk feeding has been associated with

[†]Department of Pediatric Newborn Medicine, Baystate Medical Center, Springfield, Massachusetts.

[‡]Mothers, Babies and Women's Health Program, Mater Research Institute–The University of Queensland, Aubigny Place, South Brisbane, Australia.

[¶]Department of Pediatrics, Albany Medical Center, Albany, New York.

[¥]Department of Pediatrics, Rutgers–Robert Wood Johnson Medical School, New Brunswick, New Jersey.

Accepted for publication May 9, 2017.
http://dx.doi.org/10.1016/j.clinthera.2017.05.341
0149-2918/$ - see front matter

enhanced immunity and gut maturation; decreased rates of necrotizing enterocolitis (NEC), allergies, asthma, and obesity; and improved neurodevelopmental and behavioral outcomes.[2–5] However, some mothers who deliver prematurely struggle to produce breastmilk. Historically, when MOM was unavailable or in low supply, preterm formula (PF) was the only alternative feeding option. A more recently available alternative to PF is human donor breastmilk (DBM). DBM is pooled, pasteurized breastmilk donated to milk banks by mothers with excess, primarily term, pumped milk.[6,7] DBM use has increased over the past decade and, as of 2014, over half of all US neonatal intensive care units (NICUs) offered DBM as an option in preterm infants despite its expense and limited research investigating the short- and long-term risks and benefits.[8,9]

A recent trial from the Netherlands investigated the impact of DBM on NEC and sepsis and found that DBM supplementation, compared with formula supplementation, did not decrease the rates of these morbidities.[10] However, MOM composed 85% to 90% of the infants' diet during the first 10 days of life, when the intervention was administered. Another recent trial from Canada measured the effects of DBM supplementation on infant neurodevelopment and found in a post-hoc exploratory analysis that infants randomized to DBM were more likely to have cognitive neuroimpairment (defined as a Bayley III cognitive score of <85) at 18 months compared with infants who received PF supplementation, despite no significant difference in mean cognitive scores (the primary outcome).[11] In this population, MOM composed 56% to 63% of the infants' diet, and the intervention was continued until age 90 days or hospital discharge. Notably, from the first administration, DBM was routinely fortified with extra protein. Despite varied nutritional practices, a meta-analysis of data from 9 older trials showed that supplementation with DBM, as opposed to formula, reduced the prevalence of NEC; however, it also significantly compromised growth.[12] With updated nutritional strategies, more recent studies have shown evidence both for and against the association of DBM with growth failure.[5,11,13–16]

In the extremely preterm infant, suboptimal nutrition and inadequate weight gain are linked to compromised neurodevelopmental outcomes (NDOs).[17–19] Ehrenkranz et al[17] identified a strong relationship between poor in-hospital growth and compromised NDOs at age 18 to 22 months. Stephens et al[18] demonstrated that optimized protein intake during the first week of life confers later cognitive benefits: each 1-g/kg/d protein intake was associated with an 8.2-point increase in the Mental Developmental Index at 18 months. Given the routine processing that DBM undergoes and the concern for poor growth in preterm infants fed DBM, there is a need for assessing the impact of routine DBM use on developmental outcomes.

The aims of the present study were to understand the impact of DBM supplementation on neonatal growth, the primary outcome, and to explore the association between DBM feeding and NDOs. We hypothesized that compared with preterm infants fed MOM or PF, those fed predominantly DBM would have impaired growth and compromised NDOs.

PATIENTS AND METHODS

Patients and Practices

In 2011, the Tufts Medical Center NICU (Boston, Massachusetts) began to offer DBM in infants whose birthweight was <1 kg and in all multiples if at least 1 sibling's birthweight was <1 kg. Before that time, all infants received either MOM or PF, or a combination of the two. Once this DBM policy was initiated, parents were given the option of PF or DBM when MOM was unavailable or in low supply. DBM was provided only after parental consent was obtained. DBM and PF were used either as a sole enteral diet or, more commonly, as a supplement to MOM, as MOM was prioritized in each case as availability allowed. Regardless of feed type, enteral trophic feeds were initiated in all infants (whose clinical status allowed) by 3 days of life. Feeds were advanced as tolerated by 20 mL/kg/d until full feeds of 130 to 150 mL/kg/d were reached. Fortification was initiated at 100 mL/kg/d. DBM and MOM were fortified in the same way; a bovine-based fortifier was added to 24 kcal/oz, followed by protein supplementation, and, if needed, medium-chain triglycerides and hydrolyzed cornstarch were added to increase calories further to a maximum of 30 kcal/oz. PF was fortified using increasing concentrations of formula powder, as per formula instructions. In all infants, regardless of feed type, the need for fortification was determined using a