The effects of fortified donor human milk compared to fortified mother's own milk on preterm infant weight gain in the neonatal intensive care unit

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STUDY PROPOSAL AND RATIONALE

Maternal breast milk is the optimal source of nutrition for preterm infants [1]. However, a variety of factors such as insufficient milk volume, maternal medication, or maternal drug use may make providing an infant with its own mother's breast milk difficult. Donor human milk (DHM) is the alternative of choice, especially for preterm infants, in these scenarios [2,3]. DHM reduces time to full enteral feeds, culture-proven sepsis, retinopathy of prematurity (ROP), and necrotizing enterocolitis (NEC) when compared to preterm formula [4–6]. Further, an exclusive diet of breast milk promotes reduction in hospital costs [7,8].

DHM is pooled milk from mothers of term infants in various stages of lactation, and as a result, the nutritional properties of donor milk may vary from batch to batch [9]. Additionally, milk from mothers of preterm infants is more rich in protein, immunoglobulin, and electrolyte content [10]. The American Academy of Pediatrics currently recommends fortifying breast milk for infants born 1.5kg or less [2]. Fortification of breast milk contributes to greater weight gain in preterm infants [11]. It helps better meet the preterm infant's unique nutritional needs and achieves better short term growth, which is associated with improved neurocognitive outcomes [12]. Unfortified DHM, like a mother's own milk (MOM), has been associated with slower neonatal growth when compared with PF.

More narrowly, some studies demonstrate that DHM contributes to slower growth of preterm infants in the immediate postnatal period compared to MOM [5,13]. These studies, however, primarily include unfortified DHM, or DHM with bovine milk-based fortifier. More recent studies have begun to show that a diet consisting of an exclusive human milk-based utilizing human milk-based fortifier leads to growth meeting targeted standards [14]. Therefore, given that diets consisting of exclusively breast milk are associated with decreased morbidity and decreased hospital costs, we must further investigate how preterm infants who consume DHM fortified with human milk-based fortifiers grow compared to infants who consume MOM fortified with human milk-based fortifiers.

AIM:

The aim of this study within the neonatal intensive care unit (NICU) is to measure the growth velocity (grams / kilogram / day) of preterm infants who consume MOM fortified with human milk-based fortifier, compared to preterm infants who consume DHM fortified with human milk-based fortifier.

HYPOTHESIS:

We hypothesize that that preterm infants who exclusively consume MOM fortified with human milk-based fortifier have a growth velocity that is not statistically different from preterm infants who exclusively consume DHM fortified with human milk-based fortifier.

STUDY DESIGN

This is a retrospective study within the NICU at the New York-Presbyterian Morgan Stanley Children's Hospital of New York within Columbia University Irving Medical Center. Donor human milk through the donor milk program has been available since January 2016. Donor milk is available with maternal consent to all premature infants meeting the following criteria: birth weight <1500g, gestational age at birth <34 weeks. Growth velocity with be evaluated in infants within the study groups admitted to the

NICU contemporaneously. Evaluation of growth velocity begins once infants have regained their birth weight and are also on "full feeds" (defined as 120kcal/kg/d, via a volume of 150ml/kg/d of milk fortified to 24kcal/oz). Of note, unfortified DHM and unfortified MOM is estimated to contain 20kcal/oz. For purposes of analysis, we will assess growth velocity of infants in each group while they are exclusively fed MOM or DHM via bottle or nasogastric tube (NGT). If an infant has been on an exclusive diet of DHM, for example, at one point during their admission, and an exclusive diet of MOM, for example, at another point during their admission, the infant will be assigned to initial diet. Infants who have had NEC, surgery, or cardiac conditions aside from PDA will be excluded from analysis.

STUDY SUBJECTS

Study subjects broadly include preterm infants consuming either MOM with human milk-based fortifier, or DHM with human milk-based fortifier born <1500g or <34 weeks gestation. As the DHM program was initiated in January 2016, only infants born after January 2016 will be eligible. For purposes of analysis, we will assess growth velocity of infants in each group while they are exclusively fed MOM or DHM via bottle or nasogastric tube (NGT). An infant will be assigned to study group (MOM or DHM) based on the diet on which they initially achieved "full feeds" after regaining birth weight. An infant may only belong to one study group. Infants who have had NEC, surgery, or cardiac conditions aside from PDA will be excluded from analysis.

STATISTICAL ANALYSIS

The primary outcome is to detect a difference in growth velocity (grams / kilogram / day) between the two study groups. Given an expected growth velocity of 15g/kg/d, power analysis using unpaired t-test to detect a difference between means (MOM vs DHM) of 2g/kg/d, a sample size of 64 infants in each group should be sufficient with 80% power using an alpha value of 0.05.

RECRUITMENT OF SUBJECTS

No recruitment of subjects will occur as this is a retrospective chart review.

STUDY PROCEDURES, DRUGS, OR QUESTIONNAIRES

No procedures will be performed. No drugs, devices, or questionnaires will be studied.

CONFIDENTIALITY OF STUDY DATA

Study data will be stored in a secure database located on NYP/CUMC hospital computers. Only study investigators who have completed the appropriate HIPAA and clinical research training will access data. Any unneeded identifying information will be removed from the database once data collection is complete.

POTENTIAL CONFLICTS OF INTEREST

None of the investigators have any conflict of interest to report.

LOCATION OF STUDY

The NICU at the New York-Presbyterian Morgan Stanley Children's Hospital of New York within Columbia University Irving Medical Center.

POTENTIAL RISKS

There are no potential risks for this retrospective chart review except the possibility of loss of confidentiality. However, this risk will be minimized by limiting access to the database to qualified study personnel, maintaining the data on secure network encrypted devices, limiting the identifying data

abstracted from the medical record; and removing any unnecessary identifying information from the database as soon as possible.

POTENTIAL BENEFITS

As a retrospective chart review, there are no immediate benefits to the patients in this study. The information gained from this study may have an impact on the feeding practices of preterm infants in the NICU, which may in turn reduce morbidity associated with prematurity.

ALTERNATIVE THERAPIES

Growth velocity of infants consuming formula will not be analyzed.

COMPENSATION/COSTS TO SUBJECTS

No compensation or additional cost to subjects as this is a retrospective study.

RADIATION OR RADIOACTIVE SUBSTANCES

This study will not employ radiation or radioactive substances.

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