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Effect of donor milk supplementation on breastfeeding outcomes in term newborns, a randomized controlled trial

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Abstract

Background: Pasteurized donor human milk (DHM) use for healthy newborns is increasing; however, no studies have explored its effect on breastfeeding outcomes.

Patients and Methods: We enrolled 60 healthy, term breastfeeding newborns with ≥4.5% weight loss in the first 36 hours in a randomized controlled trial. 30 were randomly assigned to early limited-volume DHM supplementation, 30 to exclusive breastfeeding. Mothers were surveyed at 1 week, 1, 2, & 3 months, regarding mode of infant feeding. Comparing infants randomized to DHM supplementation to those exclusively breastfeeding, there was no significant difference in the proportion using formula at 1 week (21% vs 7%, p=.15), nor in the proportion of any BF (79% vs 90%, p=.30) or BWF at 3 months (62% vs 77%, p=.27).

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Contributors' Statements:

Dr. Kair conceptualized and designed the study, oversaw recruitment and data collection, performed the analysis, and drafted the initial manuscript.

Drs. Colaizy and Flaherman assisted with study design, assisted with interpretation of results, and critically reviewed and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Conclusion: For newborns with ≥4.5% weight loss in the first 36 hours, early limited-volume supplementation with DHM is unlikely to have a significant favorable impact on breastfeeding outcomes.

Keywords

Donor human milk; breastfeeding; breast milk; neonate; donor milk; milk banking

Introduction

Use of pasteurized donor human milk (DHM) in the well newborn population has become increasingly common over the last two decades [1–3]. This is in part due to concerns that formula use in the neonatal period is associated with decreased breastfeeding duration as well as concerns about the effect of exposure to formula on infant intestinal microbiota and oxidative stress [4–7]. In alignment with recommendations by the World Health Organization (WHO) and the American Academy of Pediatrics (AAP), the Joint Commission Perinatal Care Measures call for avoiding formula use for breastfed infants during the birth hospitalization but do not discourage the use of DHM.[8,9] Infants who receive DHM meet the definition of exclusively breast milk fed used by these groups.

Although these public health recommendations all support the use of donor milk for healthy term infants, no published studies have explored the effect of DHM supplementation during the birth hospitalization on outcomes for this population. In contrast, a variety of studies have examined the impact of formula supplementation during the birth hospitalization. While many observational designs have demonstrated an association between in-hospital formula use and shortened breastfeeding duration, controlled trials exploring this relationship have not reported similar results; [10,11] DHM supplementation might have an impact on breastfeeding that is similar to, or different from, formula. We set out to explore the effect of early, small-volume, banked DHM supplementation prior to maternal mature milk production on formula use at 1 week and rates of any and exclusive breastfeeding at 3 months. We hypothesized that for infants with a high first-day weight loss, short-term supplementation with small volumes of donor human milk prior to maternal mature milk production would bridge dyads through the challenges of breastfeeding prior to maternal mature milk production and would lead to decreased formula use at 1 week of age and increased rates of breastfeeding and breastfeeding without formula supplementation at 3 months.

Materials and Methods

Setting

Between August 2014-June 2016 we enrolled in a randomized controlled trial 60 healthy, term breastfeeding newborn infants and their mothers cared for in the mother baby unit in a suburban academic medical center. This study was approved by the Institutional Review Board and was registered at clinicaltrials.gov (NCT02221167). All participant mothers gave written informed consent.

Participants

Inclusion criteria included infant gestational age ≥37 weeks, weight loss ≥ 4.5% from birth weight by 36 hours of age, and chronologic age of 24–48 hours at the time of enrollment. The value of 4.5% weight loss was chosen because previous evidence suggests that infants with this degree of weight loss in the first day are at a significantly increased risk of eventual weight loss >10% of birth weight [12], a frequently used threshold for excessive neonatal weight loss [13]. Infants were excluded if they had received >1 formula or DHM supplement prior to enrollment, had chromosomal or craniofacial anomalies that might interfere with breastfeeding (trisomy 21, cleft lip and/or palate, micrognathia, ankyloglossia), were admitted to the neonatal intensive care unit, had lost ≥10% from birth weight, or if their mother was <18 years old, incarcerated, unable to speak or read in English, or indicated she had already experienced the onset of mature milk production.

Recruitment

A study investigator (research nurse or principal investigator) screened infants for eligibility using the electronic medical record. Potentially eligible dyads were approached in the mother's hospital room. The study investigator discussed the study with eligible mothers and sought their consent. While describing the study to parents, prior to obtaining written informed consent, the study investigator explained that for infants randomized to the intervention group, parents would provide donor human milk supplementation via syringe, and for infants randomized to the control group, parents would be advised to continue exclusive breastfeeding unless otherwise directed by their clinicians. Written informed consent to participate was obtained from the mothers.

Randomization

Prior to enrollment of the first participant, an investigator unaffiliated with the study generated a block randomization sequence using a computer and concealed the randomization sequence in numbered opaque envelopes. Immediately following obtaining consent, the study investigator opened the next opaque envelope in the sequence to reveal treatment assignment.

Interventions

Infants randomly assigned to the intervention group were instructed to continue maternal breastfeeding and to supplement after each maternal breastfeeding with 10 mL DHM fed via finger-feeding with a syringe, until the onset of maternal milk production, identified by a validated technique [14]. The study investigator met with the mother each subsequent day until hospital discharge and inquired whether her mature milk had come in. At the time of hospital discharge, mothers whose mature milk had not yet come in received 200 mL DHM in a breast milk storage cooler for home use. All mothers were instructed to discontinue DHM supplementation and resume exclusive breastfeeding at the onset of mature maternal milk production. Infants randomly assigned to the control group were advised to continue exclusive breastfeeding unless otherwise directed by their health care providers. A study investigator met with mothers in the control group daily while they were inpatient and asked

whether their mature milk had come in. At the time of hospital discharge, mothers in the control group received a breast milk storage cooler.

Blinding

Study investigators, participants, and the medical teams caring for participant infants and mothers were not blinded to study group.

Outcome Measures and Follow-up

The primary outcome of this study was formula use at 1 week, and secondary outcomes were prevalence of any breast milk feeding and breastfeeding without formula use at 1, 2, and 3 months. Structured telephone interviews were completed at 1 week and at 1, 2, & 3 months. Any breast milk feeding was defined by a mother answering “yes” in response to items querying about whether she had, in the past 24 hours, breastfed directly, fed her own expressed milk, and/or fed DHM. Exclusive breast milk feeding was defined by a mother answering “yes” to items querying about whether she had, in the past 24 hours, breastfed, fed her own expressed milk, and/or fed DHM and “no” to an item querying about whether she had fed formula in the last 24 hours.

Power

The sample size of 60 for this study was selected for feasibility of enrollment in a 1–2 year period. We estimated that a sample size of 60 would provide a power of 80%, with alpha of 0.05, to detect a 37 percentage point difference in formula use at 1 week (from 50%, estimated from national data [15], to 13%, given the effect size seen in a previous intervention trial [10,16]. Based on effects seen previously and using alpha of 0.05, we also estimated that a sample size of 60 would provide a power of approximately 80% to detect a 37 percentage point difference in the proportion of infants breastfeeding without formula at 3 months and 66% power to detect a 27 percentage point difference in the proportion of infants receiving any breast milk at 3 months [10,16].

Analysis

Using an intention-to-treat approach, we used Chi-square or Fisher’s Exact Test analysis, as appropriate, to compare differences between the two treatment arms with respect to dichotomous outcomes, and we used Student’s t-test to compare the two groups with respect to continuous outcomes. All analyses were conducted using SPSS Statistics Version 23 (IBM Corporation, Chicago, IL).

Results

Of 397 eligible mother-infant dyads, consent was obtained from 60 (15%). (Figure 1) Of those 60 dyads, 59 completed all study activities and follow up assessments, and one (DHM group) dropped out immediately after randomization. Demographic characteristics of participants are shown in Table 2. More women who were married or lived with their partner were randomized to the control group than the DHM intervention group (100% of control mothers vs. 83% of donor milk mothers, p=0.02), and all other characteristics were similar between groups.

There were no statistically significant differences between the two groups with respect to formula use at 1 week nor with respect to any breast milk feeding or breastfeeding without formula at 1 week, 1, 2, or 3 months (Table 2). One mother in the DHM group was not breastfeeding due to health concerns at 1 month, but had resumed breastfeeding by the time of the 2-month call. The relative risks (RR) for breastfeeding cessation by 3 months and for cessation of exclusive breast milk feeding by 3 months, respectively, were 2.07 (95% confidence interval: 0.57–7.51) and 1.63 (95% CI 0.73–3.61) for the DHM group compared to the control group. Prevalence of feeding the infant at breast within the last 24 hours was lower in the DHM group than the control group (66% vs. 90% at 3 months, p=0.03, RR 3.45 with 95% CI 1.05–11.28). No significant adverse events were reported by participants in either study group.

Discussion

Our study is the first randomized trial to explore the effect of early, short-term donor milk supplementation versus exclusive breastfeeding prior to maternal mature milk production on ongoing exclusive breastfeeding in healthy, term infants. In our sample size of 60 healthy, breastfeeding infants followed for 3 months, short-term supplementation with 10 mL donor milk after each breastfeeding prior to the onset of maternal mature milk production did not demonstrate a significant impact on duration of any breast milk feeding or use of formula. However, the prevalence of feeding directly at breast (as opposed to feeding expressed breast milk without any feedings at breast) was lower in the DHM than in the control group. This result may be important, because using donor milk to supplement well newborns has become increasingly common, but no previous studies have assessed its impact on rates of maternal breastfeeding.

The use of donor milk might possibly impact well newborns in a number of potentially advantageous or deleterious ways. The potential benefits of donor milk are numerous. For those infants who would otherwise have fed formula, feeding donor milk instead of formula might provide less exposure to the potentially allergenic components of formula, and might provide greater intake of human milk oligosaccharides and glycans, thought to be important to the development of a healthy intestinal microbiota [17]. Feeding donor milk instead of formula might also help maintain maternal breastfeeding by allowing mothers to feel satisfaction in maintaining an exclusively breast milk diet for their infant; some preliminary research supports this hypothesis [2,18]. For those who would otherwise have breastfed exclusively, such as those in our study, feeding donor milk might provide additional fluid and calories that could prevent dehydration or ameliorate hyperbilirubinemia. Donor milk might also have potential disadvantages for newborns, if feeding donor milk satiates them so they do not latch or suck vigorously with their mothers or if feeding donor milk leads mothers to undervalue the provision of their own maternal milk. While DHM did not have a statistically significant impact on breastfeeding rates in our small study, a trend toward shorter duration of breastfeeding was noted in the DHM group compared to the control group (RR 2.07, 95% CI 0.57–7.51 for cessation of breastfeeding by 3 months).

Limitations

Our study also had several important limitations. First, given the low rates of breastfeeding cessation in our study population, our sample size of 60 infants could not exclude a clinically important effect of donor milk on breastfeeding outcomes. Future studies on this topic should include larger sample sizes. Second, our study was conducted in a single hospital where donor milk is already the standard-of-care supplement choice in the well newborn nursery. This may limit the generalizability of our findings. Third, only 15% of eligible mothers consented to participate in the study. If DHM has a differential impact on mothers who are open to either DHM or continued exclusive maternal breastfeeding, DHM might have had a different impact had it been used by those who declined to participate. Fourth, all five single mothers in our cohort were randomly assigned to DHM by chance. This may have introduced confounding, but the sample size of our study prohibited multivariable regression analysis.

Our study also had several important strengths, including excellent outcome ascertainment and a randomized design. While important health benefits from DHM have been identified in the high-risk, preterm infant population [19,20], our results indicate that further evaluation of the impact of donor milk on breastfeeding is needed before DHM can be recommended for use in the well newborn nursery setting. Since it is possible that the effect of donor milk on breastfeeding duration may vary based on the degree of newborn weight loss, future projects might consider categorizing newborn weight loss using published nomograms [21,22]. Assessment of the impact of donor milk supplementation on infant intestinal microbiota and allergic status may also be informative, as the benefits for infants of pasteurized, banked donor milk may not be identical to the benefits of fresh maternal milk.

Conclusion

For breastfeeding newborns with ≥4.5% weight loss in the first 36 hours, early limited supplementation with DHM is unlikely to have a significant favorable impact on breastfeeding outcomes. Future research is needed to help clarify whether healthy, full-term infants with a medical indication for supplementation would benefit from use of DHM rather than formula. Because DHM is a limited resource and significant health benefits from DHM have been identified in the high-risk, preterm population [19,20], if donor milk is inefficacious but not harmful to well newborns, it may nevertheless be important to avoid its routine use in this population so as to preserve its availability for those who will receive benefit.

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Abbreviations:

BF	breastfeeding
BWF	breastfeeding without formula
CI	confidence interval
DHM	donor human milk
RCT	randomized controlled trial
RR	relative risk

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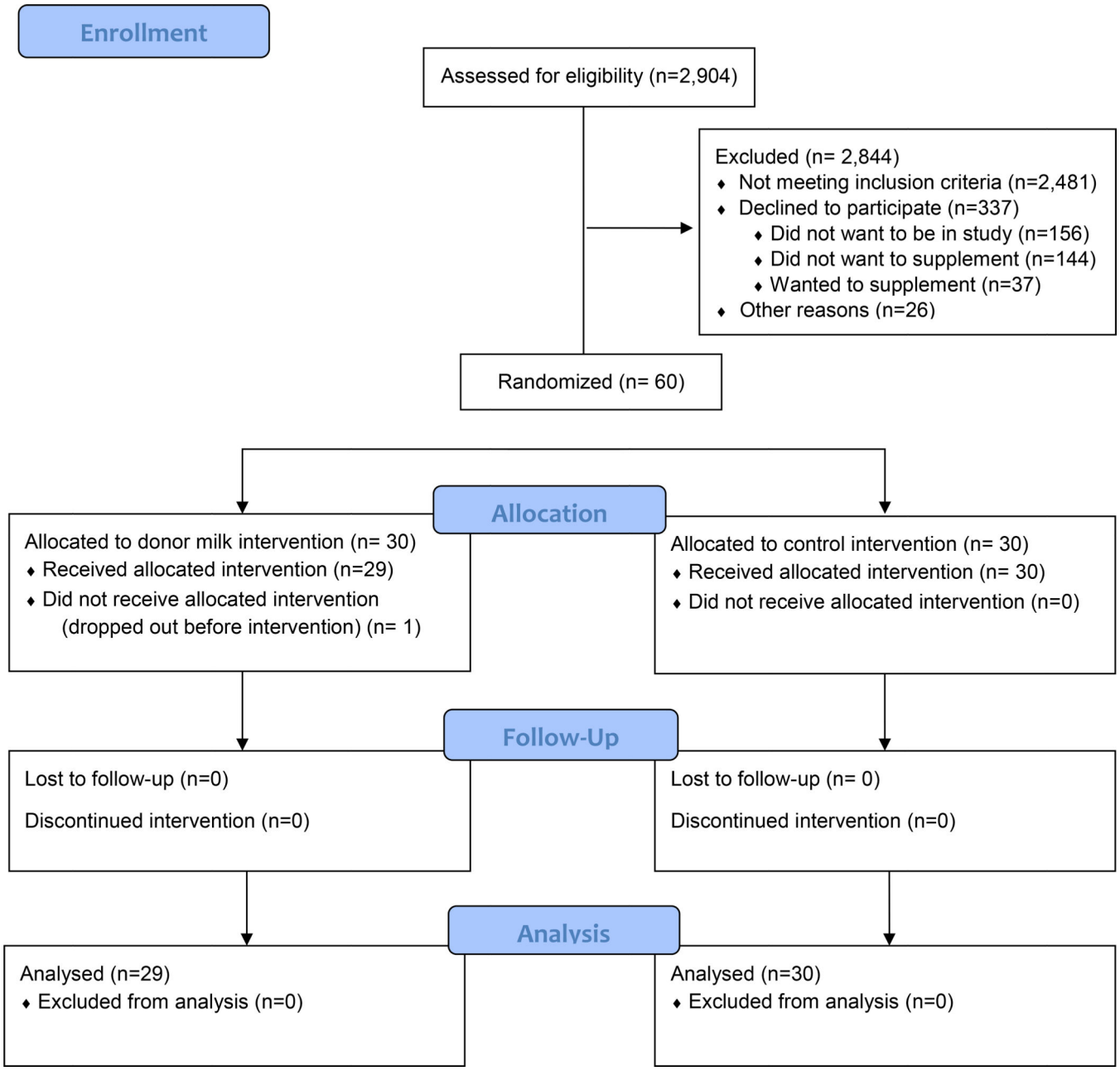

Figure 1.
Flow diagram for Rx Milk Trial

Table 1.

Demographic and Clinical Characteristics of Participating Dyads

Characteristic Mean ± SD or N (%)	Donor Milk (Intervention) Group N=29	Exclusive Breastfeeding (Control) N=30	p
Maternal age, years	30.4 ± 4.7	31.0 ± 4.5	0.63
Gestational age at delivery, weeks	39.4 ± 0.9	39.5 ± 1.2	0.76
Cesarean delivery	5 (17)	8 (27)	0.38
Race			0.18
White	24 (83)	29 (97)	
Black	2 (7)	0 (0)	
Asian	3 (10)	1 (3)	
Hispanic ethnicity	2 (7)	2 (7)	1.00
Multiparous	13 (45)	18 (60)	0.30
Married/live in partner	24 (83)	30 (100)	0.02
Insurance			0.42
Medicaid	5 (17)	3 (10)	
Private	24 (83)	25 (83)	
Medicaid + Private	0 (0)	1 (3)	
Other	0 (0)	1 (3)	
Maternal education			0.70
High school or GED	3 (10)	1 (3)	
Some college/ Associate's	6 (21)	5 (17)	
Bachelor's Degree	9 (31)	11 (38)	
Graduate Degree	11 (38)	13 (43)	
Planning to use formula	6 (21)	5 (17)	0.75
Male infant	18 (62)	13 (43)	0.20
Weight loss % at enrollment	5.9 ± 1.1	5.8 ± 1.2	0.88
Hour of age weight loss measured	27.0±5.9	27.3±6.4	0.88
Breastfeeding self-efficacy	50±12	49±9	0.75
Maternal pain			
Breast	1.3±1.5	1.8±1.7	0.30
Abdominal	2.0±2.6	2.3±2.1	0.55
Back	1.1±1.9	0.9±1.7	0.67
Vaginal	2.3±2.2	2.5±2.5	0.76

Table 2.

Infant feeding outcomes

Feeding outcome	Donor Milk (Intervention) Group N=29	Exclusive Breastfeeding (Control) N=30	p
Any formula use			
1 week	6 (21)	2 (7)	0.15
1 month	9 (31)	5 (17)	0.23
2 months	9 (31)	6 (20)	0.38
3 months	11 (41)	7 (23)	0.27
Any donor milk use			
1 week	4 (14)	1 (3)	0.20
1 month	1 (3)	0 (0)	0.49
2 months	1 (3)	0 (0)	0.49
3 months	0 (0)	0 (0)	-
Feeding at breast *			
1 week	26 (90)	29 (97)	0.35
1 month	21 (70)	29 (97)	0.01
2 months	21 (70)	27 (90)	0.10
3 months	19 (66)	27 (90)	0.03
Feeding mother's expressed milk			
1 week	8 (27)	9 (30)	1.00
1 month	13 (45)	13 (43)	1.00
2 months	13 (45)	19 (63)	0.20
3 months	18 (62)	18 (60)	1.00
Any breast milk feeding **			
1 week	28 (96)	30 (100)	0.49
1 month	23 (79)	29 (97)	0.05
2 months	24 (83)	28 (93)	0.25
3 months	23 (79)	27 (90)	0.30
Breastfeeding without formula ***			
1 week	23 (79)	28 (93)	0.15
1 month	20 (69)	25 (83)	0.23
2 months	20 (69)	24 (80)	0.38
3 months	18 (62)	23 (77)	0.27

* feeding at breast means the infant breastfed directly at breast within the last 24 hours

** any breast milk feeding means the infant received mother's own milk at breast, mother's own pumped or expressed milk, and/or donor human milk in the last 24 hours

*** breastfeeding without formula means the infant received mother's own milk at breast, mother's own pumped or expressed milk, and/or donor human milk and did not receive formula in the last 24 hours