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Original article

Mother's own milk versus donor human milk: effects on growth and outcomes in preterm neonates

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Abstract

Introduction: The present study compares the effects of mother's own milk (MOM) and donor human milk (DM) on anthropometric indices, incidence of sepsis, necrotizing enterocolitis (NEC), and feeding intolerance (FI) among preterm neonates.

Methods: Ninety neonates born at 30-32 weeks and hospitalized in the Neonatal Intensive Care Unit were assigned to 3 groups based on their daily milk intake. The first group received only MOM or < 20% DM, the second group received ≥ 20% to < 80% DM, and the third group received ≥ 80% DM.

Results: Weight gain velocity was 1.5 g/kg/day in the group that received ≥ 80% DM and 6.2 g/kg/day in the group that received 80-100% MOM (without a statistically significant p-value). Furthermore, there was no statistically significant difference in height increase among the 3 groups, and no sepsis or NEC were observed in any of the 3 groups either. The incidence of FI was not significantly different among the 3 groups.

Conclusion: Based on the results, DM is as effective as MOM in preventing sepsis, NEC, and FI. Every effort should be made to educate mothers on this subject, provide breastfeeding support, and use pasteurized and appropriately fortified DM.

Keywords

Donor human milk, feeding intolerance, mother's own milk, growth, necrotizing enterocolitis, sepsis.

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Introduction

Breast milk is recommended as the best nutrition for all newborns, especially preterm neonates. The American Academy of Pediatrics states that when mother's own milk (MOM) is unavailable or, in very rare cases, contraindicated, pasteurized donor human milk (DM) is an appropriate option for preterm neonates [1, 2]. MOM improves neurodevelopment outcomes among preterm neonates and reduces the risk of hypertension in adolescence [3, 4]. Moreover, preterm neonates fed with DM tend to be less at risk of develping necrotizing enterocolitis (NEC) than those fed with infant formula [5, 6]. Pasteurization process reduces the content and function of some host defense proteins and their cellular elements [1, 2]. Therefore, most DM recipients are neonates weighing less than 1,500 g [7]. DM is frozen and cultured after thawing, then pasteurized by heating to 62.5°C for 30 minutes, and is then ready to use in the absence of bacterial growth within 48 hours. Pasteurization is necessary for inactivating most viral and bacterial agents and, despite its impact on several nutritional properties, retains many of the beneficial and protective effects of breast milk [8]. DM provided by mothers who have delivered a preterm neonate contains significantly higher concentrations of protein, sodium and chloride compared to the DM of mothers who have delivered a term neonate, and consequently, it is more appropriate for preterm infants [9]. Although infants fed with DM seem to have lower weight gain than those fed with infant formula [10-13], the early initiation of feeding with fortified MOM or fortified DM is associated with improved in-hospital head growth and weight gain in very low birth weight (VLBW) infants [14]. A study conducted on 281 infants under 1 year of age who received DM during hospitalization concluded that pasteurized DM is a low-cost intervention compared to many other interventions for the care of hospitalized infants [15].

Given that preterm neonates are at a high risk of delay in neurocognitive development and other abnormalities, any intervention improving their developmental ability and growth is regarded as useful. Although lots of research are carried out worldwide for comparing MOM to infant formula or DM to infant formula, few studies have compared MOM with DM. Accordingly, the present study aimed to compare the effect of MOM and DM on growth indices and some outcomes of preterm neonates.

Methods

The present study was conducted over 10 days on 90 preterm neonates born at 30-32 weeks who were hospitalized in the Neonatal Intensive Care Unit (NICU) of Al-Zahra Therapeutic-Educational Center in Tabriz, northwest of Iran. The infants were divided into 3 groups: the first group received only MOM or < 20% DM; the second group received ≥ 20% to < 80% DM; and the third group received ≥ 80% DM. The inclusion criteria were gestational age of 30-32 weeks and age of 3-7 days at the time of study. The exclusion criteria were total or partial parenteral nutrition, severe respiratory distress requiring ventilator, severe metabolic disorders, or grade 3 or 4 intraventricular hemorrhage.

Sample size

The sample size was calculated according to the study by Montjaux-Régis et al. and based on the daily weight gain variable [16]. Considering $M_1 = 12.3$, $SD_1 = 3.9$, $M_2 = 18$, $SD_2 = 7.0$, $\alpha = 0.05$, $\beta = 0.2$, and taking account of a potential 15% attrition, a sample of 90 was estimated.

Sampling

This research is a prospective cohort study examining the effect of feeding with MOM and DM on anthropometric indices, incidence of sepsis, and NEC, as well as feeding intolerance (FI), among 3 groups of neonates. Sampling was

carried out after obtaining a code of ethics from the Ethics Committee of Tabriz University of Medical Sciences (11399.24.IR.TBZMED.REC). The researcher provided the parents with thorough information about the objectives, methods, and benefits of participating in the study. The eligible neonates' parents completed written informed consent forms.

The neonates' weight was measured without clothes and with diapers at the beginning of the study, daily in the morning shift, and after feeding in the ward. Head circumference and height of the neonates were measured at the beginning of the study and on day 10. The neonates' height while lying in the supine position and head circumference were measured using a fabric measurement tape, as this tape covered the most prominent part of the occiput up to the top of the eyebrows. All the measurments were performed by the first author (M.A.).

A daily DM intake chart was completed in each shift by the staff of the NICU to determine the percentage of DM received daily by the neonates. The amount and type of milk received at each feeding were documented in the chart.

The first author (M.A.) completed the checklist on the incidence of sepsis, NEC, FI to MOM or DM.

From the onset of sampling, each preterm neonate was assigned (by the neonatologist, M.M.G.) into one of the 3 groups based on the amount of DM received. Assignment to each group was based on the mother's milk avalability. The first group was completely fed with MOM or received < 20% DM, the second group received ≥ 20% to < 80% DM, and the third group received ≥ 80% DM for daily nutrition [16]. The DM was taken from the human milk bank at Al-Zahra Hospital. Mothers who have extra milk, regardless of whether they have had term or preterm neonates, can give DM to the human milk bank.

Statistical analysis

SPSS® v. 21 software was used for the data analysis. The normality of the data distribution was investigated using the Shapiro-Wilk test. The ANCOVA was used to compare anthropometric indices after controlling the confounding variables.

In order to calculate the neonates' weight gain velocity (WGV), the resulting weight on the 10th day of the study was divided by the weight on the 1st day of the study divided by 10, and the resulting number was multiplied by 1,000. The unit of the resulting number was g/kg/d. The logistic regression was used to compare the incidence of FI.

Results

The present study was conducted from April 2020 to April 2021. The characteristics of newborns involved in our study (tot. 90 newborns) are presented in **Tab. 1**. One of the neonates with patent ductus arteriosus died at the end of the study, but his data was included in the study similar to the other neonates. All the newborns received antibiotics, none of them were formula fed, and no newborn developed NEC or sepsis during the study (**Tab. 1**).

The results show that the data had a normal distribution.

Tab. 2 and **Tab. 3** show the evaluated outcomes and WGV during the study period.

Table 1. Characteristics of newborns involved in our study (tot. 90 newborns) and outcomes based on the proportion of donor human milk (DM).

	MOM or < 20% DM (n = 38)	≥ 20% to < 80% DM (n = 28)	≥ 80% DM (n = 24)	p-value
Gestational age (weeks), mean (SD)	31.1 (0.7)	31.1 (0.7)	31.4 (0.7)	0.337 [a]
Female, n (%)	22 (57.9)	13 (46.4)	15 (62.5)	0.473 [b]
Birth weight (g), mean (SD)	1,506.8 (326.5)	1,603.9 (462.2)	1,506.3 (313.6)	0.517 [a]
Height at birth (cm), mean (SD)	40.5 (3.0)	40.5 (3.5)	41.0 (2.7)	0.762 [a]
Head circumference at birth (cm), mean (SD)	29.0 (1.3)	29.9 (1.2)	29.3 (1.9)	0.352 [a]
Apgar score at 5 minutes, mean (SD)	8.4 (2.3)	8.1 (1.2)	7.6 (1.4)	0.261 [a]
Cesarean section, n (%)	36 (94.7)	27 (96.4)	21 (87.5)	0.394 [b]
Receiving surfactant, n (%)	34 (89.5)	23 (82.1)	16 (66.7)	0.081 [a]
Age at the start of study (days), mean (SD)	4.5 (1.6)	4.7 (1.5)	4.7 (1.7)	0.843 [a]

DM: donor human milk; MOM: mother's own milk; SD: standard deviation.
[a] One-way ANOVA; [b] Chi-square test.

Table 2. Outcomes and anthropometric indices investigated (tot. 90 newborns) during the period of study.

	MOM or < 20% DM (n = 38)	≥ 20% to < 80% DM (n = 28)	≥ 80% DM (n = 24)	p-value
Daily milk intake during 10 days (mL), mean (SD)	850.1 (423.5)	875.5 (448.8)	884.4 (462.1)	0.950 [a]
Weight on the 1st day of study (g), mean (SD)	1,424 (295.8)	1,508.7 (427.7)	1,402.9 (201.1)	0.442 [a]
Weight on the 10th day of study (g), mean (SD)	1,570.9 (360.2)	1,559.5 (393.3)	1,538.9 (287.3)	0.942 [b]
Height on the 10th day of study (cm), mean (SD)	41.0 (2.9)	40.9 (3.4)	41.6 (2.7)	0.671 [b]
WGV (g/kg/day), mean (SD)	6.2 (9.5)	4.6 (9.3)	1.5 (9.6)	0.172 [b]
FI, n (%)	8 (21.1)	6 (21.4)	2 (8.3)	0.368 [b]

DM: donor human milk; FI: feeding intolerance; MOM: mother's own milk; SD: standard deviation; WGV: weight gain velocity.
[a] One-way ANOVA; [b] ANCOVA.

Table 3. Weight and height gains (tot. 90 newborns) during the period of study.

	AMD (SE)	95% CI	p-value [a]
Total weight gain on the 10th day (g)			
MOM or < 20% DM	-	-	-
≥ 20% to < 80% DM	6.1 (31.6)	-71.0 to 83.2	0.996
≥ 80% DM	64.5 (34.2)	-18.9 to 147.6	0.178
WGV (g/kg/day)			
MOM or < 20% DM	-	-	-
≥ 20% to < 80% DM	0.2 (2.0)	-4.8 to 5.3	0.999
≥ 80% DM	4.1 (2.3)	-1.1 to 9.8	0.164
Total height gain on the 10th day (cm)			
MOM or < 20% DM	-	-	-
≥ 20% to < 80% DM	0.4 (0.1)	-0.2 to 0.3	0.334
≥ 80% DM	0.1 (0.1)	-0.4 to 0.2	0.201

AMD: adjusted mean difference; DM: donor human milk; MOM: mother's own milk; SE: standard error; WGV: weight gain velocity; 95% CI: 95% confidence interval.
[a] Considering birth weight and height as confounding variables.

Discussion

This cohort study compared the effect of MOM and DM on anthropometric indices, incidence of sepsis, FI, and NEC among neonates admitted to the NICU. The results demonstrated that, although the weight gain difference between the 3 groups was not statistically significant, WGV was lower in the group that received ≥ 80% DM (1.5 g/kg/day) than in the group receiving 80-100% MOM (6.2 g/kg/day).

Montjaux-Régis et al. in 2011 compared 3 groups of infants, including infants receiving < 20% MOM, ≥ 20 to < 80% MOM, and ≥ 80% MOM. They reported that MOM-fed infants gained more weight than DM-fed infants although there was no difference in linear growth among the 3 groups. The results revealed that the average WGV until the infants reached the corrected age of 32 weeks was 11.4 g/kg/day in the group who received < 20% MOM and 15.6 g/kg/day in the group that received ≥ 80% MOM [16].

de Halleux et al. conducted a retrospective study to evaluate growth among preterm infants. In their investigation, 37 infants received at least 75% MOM, 33 received 75% DM or more, and 31 received 26-74% DM for their daily nutrition. Based on the results, weight ($p = 0.002$) and height ($p = 0.020$) were significantly higher in the group receiving mostly MOM than the group that had received mostly DM. Nonetheless, head circumference ($p = 0.120$) was not significantly different between the two groups [17].

In another study, Brownell et al. in 2018 showed that infants who received a large amount of DM were more likely to develop postnatal growth restriction. Furthermore, increased DM consumption was associated significantly with the reduced growth velocity of head circumference. Nonetheless, there was no relationship between the proportion of DM consumption and height growth velocity [18].

In the present study, none of the neonates developed sepsis and NEC. The results of the logistic regression analysis demonstrated no significant difference in the incidence of FI among the neonates. The findings of similar studies have shown no significant differences between DM-fed newborns and MOM-fed newborns in terms of sepsis, NEC, and FI [16-18].

One of the possible causes of the reduced WGV in neonates fed with DM is the different nutrients contained, especially the protein content of MOM and DM. Pasteurization reduces the concentration of biologically active components, such as immune factors, hormones, growth factors, and water-soluble vitamins. Protein is important for growth and development, and the amount of protein in preterm raw milk at the first weeks of life is up to twice as much as in term milk [19]. Lipids and long-chain unsaturated fatty acids in preterm raw milk are higher than those in term milk, which

decrease after pasteurization due to the deposit on the wall and bottom of the container. Moreover, bile salt-stimulated lipase (BSSL), which affects fat absorption and growth, is inactivated effectively through pasteurization, and the loss of fat absorption significantly reduces the resultant energy and growth [20].

Weight is the most sensitive indicator of a newborn's growth and its measurement is considered one of the ways to assess one's health. Nearly 50% of deaths among children occur in the neonatal period, and low birth weight (LBW) is regarded as one of the main causes of neonatal mortality, since about 80% of deaths occur in preterm and LBW newborns. Preterm and LBW neonates are an at-risk group in the society, experiencing more physical and mental problems compared to normal newborns [21, 22].

The incidence of sepsis, NEC, and FI were other outcomes of the present study. The results indicated that the incidence of sepsis and NEC among neonates in all 3 groups was 0 at the end of the study period. Up to 20% of deaths in VLBW neonates are due to sepsis, and neonates with sepsis are approximately 3 times more likely to die than neonates without sepsis [23]. In addition, neonatal sepsis is the leading cause of disease and poor neural growth in VLBW neonates [24].

Sepsis occurs as early-onset sepsis and late-onset sepsis. Some factors such as low gestational age, LBW, low Apgar scores, and maternal chorioamnionitis increase the risk of early-onset sepsis [25]. Furthermore, NEC is the most common dangerous gastrointestinal emergency in the neonatal period. The incidence of NEC is about 1-5% in neonates admitted to the NICU. NEC-induced mortality and morbidity rates increase with the reduction of birth weight and gestational age [26].

Providing adequate and safe nutrition from the earliest hours of life is considered one of the most challenging tasks in caring for preterm newborns [27]. An appropriate nutrition plays an important role in the health of preterm neonates. Feeding tolerance refers to the newborn's ability to ingest and digest milk without complications, such as aspiration of milk into the respiratory tract, onset or worsening of apnea, and onset of NEC. FI is in fact very common among preterm neonates [28]. The most common symptoms of FI are gastric residual, abdominal distention, and the onset of an apnea/bradycardia crisis. Gastric residual is probably a symptom of delay in intestinal motility among VLBW infants [29-31]. Some unfortunate consequences of FI include non-optimal nutrition, decreased enteral nutrition, delayed complete intestinal nutrition, and prolonged intravenous feeding [32]. In the present study, a total of 16 cases of FI occurred, including 8 cases (21.1%) in the group that had received < 20% DM, 6 cases (21.4%) in the group receiving ≥ 20% to < 80% DM, and 2 cases (8.3%) in the group with ≥ 80% DM; however, the difference was not statistically significant ($p = 0.368$). Although the p-value did not show a significant difference, the prevalence of FI among newborns who had recived ≥ 80% DM was considerably lower.

Conclusion

The results of the present study suggest that the use of DM for feeding preterm newborns is as effective as MOM in preventing sepsis, NEC, and FI. Accordingly, decision-making about the health of preterm neonates should prioritize educating the mothers and providing breastfeeding support and using pasteurized and appropriately fortified DM. Future studies are recommended to extend their follow-up period until the age of 1 year so as to evaluate the effect of feeding type on later growth.

Limitations

One of the limitations of the present study was the small sample size, making the generalization of the results difficult. Also, randomization was not possible in this study due to ethical considerations.

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Declaration of interest

The Authors declare that there is no conflict of interest.

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