Examining weight gain: A retrospective study on preterm newborn growth on a diet exclusively of fortified donor breast milk

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Abstract. Preterm newborns born at <32 weeks gestational age are at an increased risk of developing multiple comorbidities. When a mother's own milk is unavailable as a source of nutrition, pasteurized donor breast milk may be used as a substitute. Recent studies using fortified donor breast milk have demonstrated that post-natal growth may be achieved comparable to a mother's own milk. Using data from our milk laboratory charts of preterm newborns exclusively fed fortified donor breast milk, the present study focused on weight gain in relation to the volume of feeds received. The micro-preemie group averaged feeds at the goal volume of 140-170 ml/kg/day for 34% of the time, with the weight gain goal of 15-20 g/kg/day met 30% of the time on average. The extremely low birth weight group averaged feeds at the goal volume of 140-170 ml/kg/day for 70% of the time, with the weight gain goal of 15-20 g/kg/day met 34% of the time on average. The very low birth weight group averaged feeds at the goal volume of 140-170 ml/kg/day for 56% of the time and achieved the weight gain goal of 15-20 g/kg/day 21% of the time, on average. On the whole, the findings of the present study indicate that standard growth goals may be realized with fortified donor breast milk fed at a goal volume.

Introduction

Preterm newborns (PTNBs) born at ≤32 weeks gestational age (GA) are at increased risk for multiple comorbidities due to immature cardiac, respiratory, renal and gastrointestinal (GI) systems (1-3). The use of a mothers' own milk (MOM) for nutrition in infants with an extremely low birth weight (ELBW), very low birth weight (VLBW) and micro-preemies is preferred over donor breast milk (DBM) (4,5). MOM provides bioactive compounds to help with biological processes (6). Growth factors in MOM enhance gut maturation and peristalsis (6). The variety of cells in MOM stimulates the development of the infant's immune system, while multi-functional peptides facilitate communication between cells to affect immune behavior (6). Prebiotics contained in MOM encourage the growth of healthful probiotics in the GI tract, possibly preventing infection and future diseases (6). Neurodevelopment may be enhanced in VLBW infants receiving a diet exclusively of MOM (7). Arachidonic acid (AA) and docosahexaenoic acid (DHA), long chain polyunsaturated fatty acids (LCPUFA), facilitate brain and vision development in the embryonic stage (8). If the maternal diet during pregnancy is deficient in AA and DHA, fetal maturation of the central nervous system may be negatively affected (8-10). It is recommended for pregnant women to consume 2 portions per week of oily fish or supplements containing DHA (10).

The use of entirely MOM for nutrition can help reduce the length of stay (LOS) of infants in the neonatal intensive care unit (NICU) by reducing the number of days on central parenteral nutrition (CPN), which in turn reduces the risk of infection (11). One of the most compelling reasons for the use of MOM for the feeding of PTNBs is the protective properties against necrotizing enterocolitis (NEC), a devastating insult to the GI tract, which can result in the delay of initiation of nutrition, growth failure, sepsis, short bowel syndrome (SBS) and even death (12). The use of pasteurized DBM (PDBM) in the NICU is an acceptable alternative to MOM, and is now prevalent, although the criteria for its use vary (13).

While retaining many of the properties inherent in MOM, the pasteurization process needed to make DBM safe for use for feeding to PTNBs can reduce or destroy some of the beneficial qualities of human milk (14). Research comparing the growth of PTNBs fed with MOM to those fed with PDBM have reported reduced growth in infants receiving the PDBM (15). Observed growth differences may be due to the variability of biological active compounds and the protein load of MOM (6). Deficits in growth may also be dose-dependent in infants receiving PDBM in combination with MOM (16), infusion practices of enteral feeds (17,18), the delay of initiation and advancement of feeds (19,20), and the fortification practices of human milk (21). Research completed recently has provided varying results in growth comparisons between the uses of MOM fortified and PDBM fortified, while research on the use of PDBM exclusively is limited (22). Human milk fortifiers (HMFs) are

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bovine-based or human milk-derived, in powder or liquid forms (23). Companies such as Prolacta (24), Medolac (25) and NiQ (26) provide donor human milk with calorie and protein-specific content. These products can be cost prohibitive for some health care facilities (27-29). Donor breast milk can also be purchased at a comparatively lower cost from a Human Milk Banking Association of North America (HMBANA), a non-profit milk banking agency where mothers donate their milk without receiving compensation (30). The donated milk is batched, analyzed for caloric content per ounce, and can then be ordered by healthcare facilities in various calorie amounts (31). It has been researched and reported that the Holder pasteurization method can reduce the macronutrient content in processed milk, specifically lipid and protein amounts, and therefore the importance of fortification is stressed (32). The purpose of the present retrospective study was to compare weight gain averages against standard weight gain goals among PTNBs in a hospital setting fed exclusively DBM purchased from an HMBANA milk bank, fortified with a bovine-based HMF. This investigation is relevant as DBM purchased from an HMBANA milk bank can be a cost-efficient measure for feeding PTNBs, while reducing the risk of NEC and providing protective properties inherent in human milk when MOM is unavailable for feeds (28). This investigation also contributes to the further understanding of the association between feeding fortified DBM (FDBM) to improve the growth rate of PTNBs (33). The advantage of using a set of feeding guidelines to schedule fortification and advance feed volumes is demonstrated in this retrospective study (34). The use of feeding guidelines further implements standardized practice and continuity between multiple healthcare professionals caring for PTNBs, while also providing a tracking method for analyzing feeding intolerances and growth issues (35,36).

Materials and methods

The present retrospective study involves an exploratory analysis of de-identified data obtained from the University of Arkansas for Medical Sciences (UAMS) hospital milk laboratory records from 2010-2014. The study was declared exempt status by the UAMS Institutional Review Board (IRB). The UAMS NICU instituted the use of donor breast milk purchased from an HMBANA milk laboratory just prior to the study. Feeds were compounded in the NICU Milk Laboratory per standardized mixing recipes for the preparation of human milk in health care facilities (37). Handwritten records of infant feed orders and mixing recipes had been retained for a period of 4 years until the implementation of electronic medical records. In addition to feed orders for each infant, hand-plotted, paper growth charts had been retained, which aided in the growth analysis of included subjects. Growth charts documenting length and head circumference (HC) were not available.

Inclusion/exclusion criteria. Inclusion criteria for the present retrospective study included PTNBs with a GA of 22-32 weeks. Infants must have received feeds of FDBM exclusively for a minimum of 3 weeks (21 days), consecutively.

Infants with any GI diagnoses, such as NEC or spontaneous intestinal perforation (SIP) were excluded from the study as were infants with organ failure, inborn errors of metabolism and genetic syndromes and chromosome anomalies. PTNBs transferred to another healthcare facility were noted and discontinued from the study. PTNBs with feeds held for a period of ≥48 h were not included in the data collection. When infants were transitioned to formula feeds or when MOM became available for use, they were determined to have completed feeds of FDBM, and data collection for those PTNBs ceased. PTNBs receiving MOM were not included in the data collection.

Data sources

Feeding orders. Recently implemented UAMS NICU feeding guidelines for fortification and advancement of feeds as presented in Table I were followed by the team in the NICU. The NICU registered dietitian (RD) and attending physicians used current practices and available evidence-based guidelines to develop the UAMS guidelines. Feeding guidelines can be used to provide a systematic method for advancing feeds volume and scheduled fortification of feeds (38). Milk was fortified using an acidified liquid HMF per the NICU feeding guidelines (39). The standardized fortification method was used to calculate the amount of HMF added to each order (40).

Data were gathered from handwritten, milk laboratory orders and records for infants receiving FDBM exclusively. The milk laboratory orders for each infant contained the volume, calorie per ounce, protein amount, and the number of feeds for each day. The number of days on FDBM was determined by the total number of milk orders for each infant. Other collected data included post conceptual age (PCA) when FDBM was initiated which was determined by the dates on milk orders.

Growth charts. Infant GA, PCA, birth weight (BW) and weekly weights were collected from hand-plotted growth charts for each infant. Recorded weights plotted on the growth charts were difficult to read at times and may have been questionable. If documented weights seemed unrealistic, clinical judgment by the PI (an RD board certified in nutrition support with >15 years of clinical experience) was used to determine whether the weight gain averages were fluid-related by using the PCA and the feeds volume received.

Calculation methods. Average volume intake was calculated using the sum feed intake for the week, divided by 7 days, then by the current weight, to yield a feed volume/kg/day average.

The average calorie intake per day was calculated using the 7-day feeding volume sum divided by 30 (30 ml=1 ounce), then multiplied by the calories per ounce, and divided by 7 days. Finally, the 7-day average calorie amount was divided by the current weight to provide calories/kg/day average intake. This weekly average of feeds intake was used because weight gain is calculated weekly (41). A cross-check to confirm caloric content and volume of feeds per kilogram was performed by using the UAMS NICU feeding guidelines, day of life (DOL) and weekly weight from the growth charts.

Average weekly weight gain was calculated by using the current weight for the week subtracted by the weight of the previous week, then divided by 7 days. Data were grouped by BW, micro-preemie (≤800 g at birth), ELBW (<1,000 g at birth) and VLBW (<1,500 g at birth), and GAs of 22-32 weeks. A descriptive analysis of the data was completed using Microsoft Excel, version 13.

Table I. UAMS NICU recommended feeding guidelines.

Recommended feeding guidelines for a birth weight <1,000 g

Days of feeds	Composition of feeds	Volume of feeds	Parenteral nutrition calories	Parenteral nutrition protein	Parenteral nutrition lipids
1	MOM/DBM	15 ml/kg/day	90 kcal/kg/day	4 g/kg/day	3.5 g/kg/day
2	MOM/DBM	15 ml/kg/day	90 kcal/kg/day	4 g/kg/day	3.5 g/kg/day
3	MOM/DBM	15 ml/kg/day	90 kcal/kg/day	4 g/kg/day	3.5 g/kg/day
4	MOM/DBM	15 ml/kg/day	90 kcal/kg/day	4 g/kg/day	3.5 g/kg/day
5	MOM/DBM	15 ml/kg/day	90 kcal/kg/day	4 g/kg/day	3.5 g/kg/day
6	MOM/DBM	30 ml/kg/day	85 kcal/kg/day	3.5 g/kg/day	3 g/kg/day
7	MOM/DBM	45 ml/kg/day	75 kcal/kg/day	3.5 g/kg/day	2.5 g/kg/day
8	MOM/DBM	60 ml/kg/day	65 kcal/kg/day	3 g/kg/day	2 g/kg/day
9	MOM/DBM	75 ml/kg/day	55 kcal/kg/day	3 g/kg/day	1.5 g/kg/day
10	MOM/DBM	90 ml/kg/day	45 kcal/kg/day	2.5 g/kg/day	1 g/kg/day
11	Add HMF to 22 cal/oz	90 ml/kg/day	40 kcal/kg/day	2 g/kg/day	0.5 g/kg/day
12	22 MOM/DBM	105 ml/kg/day	30 kcal/kg/day	1. g/kg/day	Discontinued
13	Increase to 24 cal/oz	105 ml/kg/day	25 kcal/kg/day	1 g/kg/day	
14	24 MOM/DBM	120 ml/kg/day	20 kcal/kg/day	0.5 g/kg/day	
15	24 MOM/DBM	135 ml/kg/day	Discontinued	Discontinued	
16	24 MOM/DBM	150 ml/kg/day			

Recommended feeding guidelines for a birth weight of 1,001-1,250 g

Days of feeds	Composition of feeds	Volume of feeds	Parenteral nutrition calories	Parenteral nutrition protein	Parenteral nutrition lipids
1	MOM/DBM	15 ml/kg/day	90 kcal/kg/day	4 g/kg/day	3.5 g/kg/day
2	MOM/DBM	15 ml/kg/day	90 kcal/kg/day	4 g/kg/day	3.5 g/kg/day
3	MOM/DBM	15 ml/kg/day	90 kcal/kg/day	4 g g/kg/day	3.5 g/kg/day
4	MOM/DBM	30 ml/kg/day	85 kcal/kg/day	3.5 g/kg/day	3 g/kg/day
5	MOM/DBM	45 ml/kg/day	75 kcal/kg/day	3.5 g/kg/day	2.5 g/kg/day
6	MOM/DBM	60 ml/kg/day	65 kcal/kg/day	3 g/kg/day	2 g/kg/day
7	MOM/DBM	75 ml/kg/day	55 kcal/kg/day	3 g/kg/day	1.5 g/kg/day
8	MOM/DBM	90 ml/kg/day	45 kcal/kg/day	2.5 g/kg/day	1 g/kg/day
9	Add HMF to 22 cal/oz	90 ml/kg/day	40 kcal/kg/day	2 g/kg/day	0.5 g/kg/day
10	22 MOM/DBM	105 ml/kg/day	30 kcal/kg/day	1.5 g/kg/day	Discontinued
11	Increase to 24 cal/oz	105 ml/kg/day	25 kcal/kg/day	1 g/kg/day	
12	24 MOM/DBM	120 ml/kg/day	20 kcal/kg/day	0.5 g/kg/day	
13	24 MOM/DBM	135 ml/kg/day	Discontinued	Discontinued	
14	24 MOM/DBM	150 ml/kg/day			

UAMS, University of Arkansas for Medical Sciences; NICU, neonatal intensive care unit; MOM, mothers' own milk; DBM, donor breast milk; HMF, human milk fortifier. 'Discontinued' indicates that the feed was no longer a source of nutrition.

Results

Data from 200 PTNBs were available; however, data from 61 PTNBs were included for analysis based on the inclusion/exclusion criteria described above. Micro-preemie PTNBs met the weight gain goal approximately 30% of the time during an 11-week period. Feeds at goal volume were met approximately 34% of the time. Meeting the volume intake goal for the week did not necessarily mean the PTNBs met the weight gain goal for the week, as shown in Table II. The micro-preemie PTNBs had FDBM introduced at 28-32 weeks PCA, and appear to have met growth standards the most consistently of the 3 PTNB groups. PTNBs in the micro-preemie group remained on FDBM the longest of the 3 groups ranging from 3-11 weeks, with the highest weight gain average occurring between weeks 5-8, as shown in Table II.

PTNBs in the ELBW group received FDBM over an 8-week period. Weight gain goals were met approximately

Table II. Micro-preemie PTNBs meeting intake and weight gain goals.

Week	Met intake goal, n (%)	Met weight gain goal, n (%)
1 (n=28)	2 (7)	7 (25)
2 (n=28)	7 (25)	6 (21)
3 (n=28)	17 (61)	4 (14)
4 (n=27[a])	15 (56)	11 (41)
5 (n=23[b])	12 (52)	11 (48)
6 (n=17[b-d])	5 (29)	9 (53)
7 (n=13[b])	8 (57)	7 (50)
8 (n=8[b,c])	2 (25)	5 (63)
9 (n=5[b])	3 (60)	1 (20)
10 (n=2[b])	0	0
11 (n=1[b])	0	0
12 (n=0[b])	N/A	N/A

[a]PTNBs transitioned to MOM (1 at week 4); [b]PTNBs transitioned to formula (4 at week 5; 4 at week 6; 4 at week 7; 3 at week 8; 3 at week 9; 3 at week 10; 1 at week 11); [c]PTNBs transferred to another healthcare facility (1 at week 6; 1 at week 8); [d]PTNBs with feeds held >48 h (1 at week 6). PTNBs, preterm newborns.

Table III. ELBW PTNBs meeting intake and weight gain goals.

Week	Met intake goal, n (%)	Met weight gain goal, n (%)
1 (n=17)	3 (18)	3 (18)
2 (n=17)	11 (65)	6 (35)
3 (n=17)	6 (35)	8 (47)
4 (n=14[a])	13 (93)	5 (36)
5 (n=9[a])	7 (78)	1 (11)
6 (n=4[a])	4 (100)	3 (75)
7 (n=3[a])	2 (67)	0 (0)
8 (n=2[a])	2 (100)	1 (50)
9 (n=0)	N/A	N/A

[a]PTNBs transitioned to formula (3 at week 4; 5 at week 5; 5 at week 6; 1 at week 7; 1 at week 8; 2 at week 9). ELBW, extremely low birth weight; PTNBs, preterm newborns.

34% of the time over the 8-week period. The highest average weight gain rate was observed in week 6, with 75% of the ELBW PTNBs meeting the goal, as shown in Table III. In total, 70% of the ELBW PTNBs achieved goal volume during the 8-week period. This PTNB group received the feeds that more closely followed the feeding guidelines among the three groups; however, this group ranked second in achieving weight gain goal on average. PTNBs in the ELBW group remained on FDBM between 3-8 weeks.

The VLBW group received FDBM for a 7-week period. Weight gain goals were met approximately 21% of the time. The highest rate of weight gain was observed in week 7, with

Table IV. VLBW PTNBs meeting intake and weight gain goals.

Week	Met intake goal, n (%)	Met weight gain goal, n (%)
1 (n=16)	4 (25)	3 (19)
2 (n=16)	6 (38)	2 (13)
3 (n=16)	7 (44)	5 (31)
4 (n=11[a])	6 (55)	2 (18)
5 (n=6[a])	5 (83)	1 (17)
6 (n=2[a])	1 (50)	0 (0)
7 (n=2)	2 (100)	1 (50)
8 (n=0[a,b])	N/A	N/A

[a]PTNBs transitioned to formula (5 at week 4; 5 at week 5; 4 at week 6; 1 at week 8); [b]PTNBs transferred to another healthcare facility (1 at week 8). VLBW, very low birth weight; PTNBs, preterm newborns.

50% of the VLBW PTNBs meeting the weight goal, as shown in Table IV. The VLBW group averaged 56% of PTNBs achieving goal volume over a 7-week period. PTNBs in the VLBW group remained on FDBM between 3-7 weeks.

Discussion

The present study analyzed FDBM amounts received for PTNBs with a BW <1,500 g and a GA <32 weeks. Average weight gain was compared against the average total volume of feeds received. The results of the present study are widely variable. As the original paper flowsheets were not available for examination, clinical judgement was used guided by the RD in the NICU to assess the advancement and fortification of feeds by using the handwritten milk laboratory feeding orders, which contained calorie per ounce and volume of milk ordered daily for each PTNB. Since no electronic medical records were utilized during the study interval, physician feeding orders that would have provided the prescribed amount of calories, protein and volume for the infants were not available, thus the need for scrutiny by the RD familiar with the process of feed orders and mixing recipes of human milk. According to the percentages reported above, the ELBW PTNB group met goal feeds volume more often than the micro-preemie and VLBW groups, at an average of 70% of the goal feed volume (140-170 ml/kg/day). As data were only available regarding the volume of feeds ordered and not specific fortification instructions, differences could be attributed to the ELBW group being advanced in feeding volume each day, then fortifying feeds once goal volume was achieved. Advancing to goal volume prior to the fortification of feeds allows physicians to remove central lines (as fluid needs will be supplied by feeds), thus avoiding an increased risk of bloodstream infection. According to available data for the PTNBs, the ELBW group reached weight gain goals only 34% of the time, which may be a result of suboptimal protein content in FDBM that had not been fortified to protein goal (42,43). The fortification of feeds is currently standard practice for both MOM and DBM for PTNBs due to insufficient amounts of protein content in human milk to support growth and development of the PTNB (40); however, the issue of when to fortify feeds

remains inconclusive (44). There are several methods available for the fortification of MOM and DBM. A standardized method using HMF per manufacturer instructions (ratio of fortifier to 100 ml of milk) (45), an individualized or targeted fortification method requiring analysis of milk samples using a mid-infrared spectrophotometer and then adding protein supplements to meet targeted goal intake (45), or an adjustable fortification method using lab values to adjust protein content in feeds (45). Targeted fortification methods are labor intensive and costly due to the analysis of the protein content in each milk sample. Adjustable fortification methods can also be labor intensive for nursing if additional protein is added to each feed at the bedside. Another consideration for adjustable fortification is determining whether laboratory tests used to make protein adjustments have not been influenced by medications, such as in the case of diuretic use and interpreting blood urea nitrogen (BUN) (46).

The micro-preemie group appeared to receive consistent feeds volume using the NICU feeding guidelines and achieve weight gain in an expected pattern. This finding may indicate greater adherence to feeding guidelines used in the NICU. The cautious nature of feeding the micro-preemie may be due to the undetermined tolerance when making more aggressive advances in volumes of feeds due to the immature GI tract (47).

The development of aggressive feeding protocols in the NICU may not reflect the actual implementation, which is an important consideration when evaluating growth of PTNBs (48). The fortification days of the protocol are to allow the PTNB to adjust to the increase in calories and protein while avoiding an increase in volume simultaneously, which may not be tolerated; however, fortifying and advancing feeds on the same day is acceptable with demonstrated tolerance (48). Eliminating days scheduled for the fortification of feeds in order to advance in volume may deter growth more than initially realized (49) despite the benefit of being able to remove venous access devices. The accretion of fat, protein, calcium and phosphorus occurs in the latter part of the third trimester, which affects neurocognitive development and growth (3). Consensus for the need of fortification of human milk for the PTNB has been established and is considered necessary for optimal protein delivery for neonatal development to avoid nutritional deficits (32). Further delay of these micro- and macronutrients in order to remove IV lines may have a greater effect on the nutrition status of the PTNB than currently considered (50). Lastly, there is evidence to suggest the use of standardized feeding guidelines for the advancement of feeds in the NICU (35). Continuity of care in the NICU may increase growth velocity (36); neonatologists in the NICU associated with this current study generally rotated on a weekly basis.

In conclusion, the present study revealed that growth standards can be achieved in PTNBs using FDBM at goal volume of 140-170 ml/kg/day. Human milk purchased from an HMBANA milk bank can be a cost-effective alternative to the use of formula in the NICU for PTNBs. Bovine-based HMFs have demonstrated tolerance with cautious advancement of feeds (29). Early fortification rather than late fortification may improve growth velocity. Using feeding guidelines to advance and fortify feeds may help the clinician provide a systematic approach to achieving optimal nutrition to meet established goal growth parameters.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article. Raw datasets can be made available from the corresponding author upon request in Microsoft Excel, version 13.

Authors' contributions

CA was involved in the development and design of the study. JP and RH assisted with the development and design of the study. CA led the data collection and analysis process. JP assisted with the data analysis process. CA led the development and completion of the manuscript. JP and RH contributed to the completion of the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present retrospective study involves an exploratory analysis of de-identified data obtained from hospital milk laboratory records. The study was declared exempt status by the University of Arkansas for Medical Sciences (UAMS) Institutional Review Board (IRB).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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