

Original Research Article

Role of human milk fortifier on weight gain in very low birth weight babies

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ABSTRACT

Background: Poor weight gain and postnatal growth of VLBW neonates continues to be a major problem. Breast feeding with HMF fortification show positive effect on growth. Main objective is to study the weight gain pattern in very low birth weight babies supplemented with HMF.

Methods: This is an observational study conducted in NICU, Department of Pediatrics, U.P. Rural Institute of Medical Sciences and research Saifai, India between January 2015- June 2016 for assessing the weight gain pattern in VLBW neonates supplemented with HMF.

Results: Maximum number of babies supplemented with HMF achieved the targeted weight in 8-14 days (32.2%) followed by those who attained this weight within 15-21 days (30%), 22-28 days (21.1%), <7 days (13.3%) and >28 days (3.3%) respectively. Mean time taken to achieve the targeted weight was 16.69±7.19 days.

Conclusions: We concluded that the supplementation with HMF, can result in a significant increase in growth. We demonstrated that fortification of human milk, with HMF did not cause any measured adverse effects in VLBW neonates.

Keywords: HMF, Fortification, VLBW

INTRODUCTION

Poor weight gain and postnatal growth of preterm neonates continues to be a major problem. Intrauterine growth retardation is an additional risk factor in the growth of preterm infants.

Breast milk is considered as the best food for the neonates due to its several nutritional and immunologic advantages but this has been well established that human milk is an inadequate source of protein and minerals and calories for growing premature babies.^{1,2} Very low birth weight babies need higher calories, protein and minerals to achieve adequate catch up growth.³

Nutritional management influences immediate survival as well as subsequent growth and development of VLBW infants. Even simple interventions such as early initiation of breastfeeding and avoidance of pre-lacteal feeding have been shown to improve their survival in resource restricted settings.⁴ Early nutrition could also influence the long term neurodevelopmental outcomes; malnutrition at a vulnerable period of brain development has been shown to have deleterious effects in experimental animals.⁵ Since intrauterine accretion of nutrients occurs mainly in the later part of the third trimester, VLBW infants (usually born before 32 weeks gestation) have low body stores at birth. Hence, they require supplementation of various nutrients.⁶ Even term

LBW infants who are likely to be growth restricted need higher calories for 'catch-up' growth.

These infants who are usually born before 32-34 weeks gestation have inadequate body stores of most of the nutrients. Expressed breast milk has inadequate amounts of protein, energy, calcium, phosphorus, trace elements (iron, zinc) and vitamins (D, E and K) that are unable to meet their daily recommended intakes. Hence, these infants need multi-nutrient supplementation till they reach term gestation (40 weeks postmenstrual age). After this period, their requirements are similar to those infants with birth weights of 1500-2499 grams.

On basis of available literature exclusive breast feeding with HMF fortification or exclusive breast feeding with individual supplementation of MCT oil, vitamins and minerals show positive effect on growth. For HMF fortification frequent expression of milk is required prior to the feed with KSF, whereas expression of breast milk is not needed in individual supplementation. Good hygiene is required in HMF while it is not required in individual supplementation. In present study we study the weight gain pattern in very low birth weight babies supplemented with HMF.

METHODS

This observational study was carried out in Sick Newborn Care Unit, Department of Pediatrics, U.P. Rural Institute of Medical Sciences and Research, Saifai UP, India between January 2015- June 2016 Written and informed consent was taken from parents/guardians. The study protocol was reviewed and approved by Ethics Committee of U.P. Rural Institute of Medical Sciences and research Saifai, UP, India.

Selection of cases

Infants were eligible if born 31 to 34 completed weeks gestation and 1100- 1500 grams birth weight; their mothers intended to provide breast milk and parents or guardians provided written informed consent. It was important that the infants were in-patients for enough time for the intervention to affect growth rate. Preterm infants normally remain in hospital to term or close to, so it was reasonable to assume that these infants would be in hospital for three to four weeks. All infants in the SNCU were screened for eligibility. A detailed antenatal, natal and postnatal history from the mother was taken and thorough clinical examination was done. Risk factors for sepsis were assessed as per detailed history. Neonate with major congenital malformation, gastrointestinal abnormalities critically ill or hemodynamically unstable were excluded. After including in the study HMF was started to all neonates as following.

Lactodex-HMF: Infants in this study received a human milk fortifier, Lactodex-HMF (Raptakos, Brettand Co. Ltd.) providing 1.08 g protein/100 ml EBM (Table 1).

Table 1: Approximate composition (per 1 g of powder).

Composition	Quantity
Protein	0.20 g
Fat	0.10 g
Carbohydrate	0.42 g
Vitamin C	5.00 mg
Vitamin E	837.50 mcg
Nicotinamide	230.00 mcg
Pantothenic Acid	100.00 mcg
Folic Acid	40.00 mcg
Vitamin A	60.00 mcg
Vitamin B ₆	25.00 mcg
Vitamin B ₂	20.00 mcg
Vitamin B ₁	12.00 mcg
Vitamin K	1.10 mcg
Vitamin D	0.95 mcg
Biotin	0.50 mcg
Vitamin B ₁₂	0.05 mcg
Calcium	50.00 mg
Phosphorus	25.00 mg
Chloride	4.40 mg
Magnesium	4.00 mg
Potassium	3.90 mg
Sodium	1.75 mg
Zinc	80.00 mcg
Copper	20.00 mcg
Manganese	1.70 mcg
Energy Value	3.63 kcal=15.20 k J

Administration of intervention

In standard clinical practice, fortifier is mixed with EBM before it is administered to the infant. In this study same practice was followed. Neonatal nurses fortified EBM with HMF. Every three hourly mother was called for and fresh EBM was fortified each time except in the night. The fortified EBM is then fed to the infant via the feeding tube or as katori spoon feeding.

As nasogastric tube increases the airway impedance and the work of breathing in preterm infants so only orogastric feeding was employed in our study as per the unit protocols.⁷ The feeding regimen was standardized was under the direction of the attending neonatologist.

The fortifiers were commenced when the infant's enteral intake reached at least 100 ml /kg/ day which was named as study day -1 and continued till the infant achieved weight of 1600 grams, named as study day-final, while the infant received EBM via feeding tube or KSF. Feed was given as intermittent bolus at 3 hourly intervals as per unit protocols.

All mothers were counselled and supported in expressing their own milk for feeding their infants, and it was initiated within hours of delivery so that infants got the benefits of colostrum. Feed was started at 80 mL/kg/day

and the usual daily increments were 20 mL/kg/day till they achieved a feed volume of 180 mL/kg/day.

Supplements were added at different times in the day to avoid undue increase in the osmolality.

Table 2: Recommended daily allowance (RDA) in preterm VLBW infants and estimated intakes with HMF human milk.

	RDA (Units/kg/day)	Only expressed breast milk #	At daily intake of 180 mL/kg EBM fortified with Lactodex-HMF (4g/100 mL)	At daily intake of 180 mL/kg EBM fortified with Simyl MCT oil (2ml/100ml)
Energy(Kcal)	110-135	117	144	145
Protein (g)	3.5-4.5	2.5	3.2	2.5
Carbohydrates (g)	11.6-13.2	11.6	16.8	11.6
Fat (g)	4.8-6.6	6.8	7.1	10.2
Calcium (mg)	120-140	43	223	43
Phosphate (mg)	0-90	22	112	22
Vitamin A (IU)	1330-3330	680	1228	680
Vitamin D (IU/day)	800-1000	3.5	140	3.5
Vitamin E (mg)	2.2-11	1.8	6.3	1.8
Vitamin B ₆ (mcg)	45-300	25.7	116	25.7
Folic acid (mcg)	35-100	6	150	6
Zinc (mg)	1.1-2.0	0.6	0.88	0.6
Iron (mg)	2-3	0.2	0.2	0.2

Concomitant care

All infants received clinical care and management according to the neonatal unit policies and procedures under the direction of the attending neonatologist with the only difference being the either study products.

Calculation and ordering of fortifier dose

4 g HMF was mixed with 100 mL of EBM. This was delivered, the fortifier calculated and ordered by the resident on duty.

For example, the calculation for an infant weighing 1.2 kg required a total enteral intake of 160ml/kg/day and fed 3 hourly (8 feeds a day) is as follows:

- Calculate total intake (mL/day):
1.2 kg x 160 ml/kg/day = 192 mL
- Calculate total HMF required (gm/day) where 1g HMF is to be delivered /25 mL EBM:
(192) ÷ 25 = 7.68 g
- Calculate HMF required per feed (g/feed):
7.68 ÷ 8 = 0.96 g

Fortification was to begin at an enteral intake of 100 ml/kg/day on the attending consultant's orders.

The fortifier dose was recalculated daily till infant reached a feed volume of 180mL/kg/day, according to current weight and intake.

Outcomes and assessment

Study start was defined as day of achieving feed volume of 100mL/kg/day and introduction of HMF and study end as attainment of weight 1600 grams.

Primary outcome-weight gain

The primary outcome of the study was rate of weight gain (g/kg/day). Body weight was measured with a direct reading electronic balance.

The balances were accurate to the nearest 5 grams. The accuracy of each balance was checked at least once in a month. Calibrated or standard weights were available for this purpose.

The infant was undressed; the scale was set to zero and the infant placed on the scale. The infant was then lifted; the scale was again set to zero and the infant placed back on the scale. If the weight differed by 20 g in two measurements, then a third measurement was taken.⁸⁻¹⁰ Weighing machine used for this study was-Electronic weighing machine EQUINOX BE-EQ-22 Max 20 Kg D 5 g.

Statistical analysis

Data was analysed using Microsoft Excel 2010. The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD.

RESULTS

In the present study, 92 VLBW newborns were studied. Birth weight of babies ranged from 1100 to 1490 gm. Among the study group 28.3% had birth weight 1200-1290 gm followed by 25% each in birth weight 1300-1390 gm and 1400-1490 gm category and only 21.7% with birth weight 1100-1190 gm. Mean birth weight of babies was 1292.5±107.5 gm. Majority of babies were males. Proportion of females was 43.5%. GA at birth ranged from 31 weeks to 33 weeks 6 days.

Majority of babies had gestational age ≤32 weeks at birth. Overall, a total of 56.5% babies had gestational age ≤32 weeks at birth whereas remaining 43.5% babies had gestational age >32 weeks at the time of birth. Mean gestational age was 32.28±0.90 week. Majority of cases were SGA. There were 47.8% AGA. These data are shown in Table 3.

Table 3: Distribution of babies according to sex and GA.

	Numbers	Percentage
Gender		
male	52	56.5
female	40	43.5
GA (weeks)		
≤32 weeks	52	56.5
>32 weeks	40	43.5
SGA	48	52.2
AGA	44	47.8

Majority of cases (62.0%) achieved full feed within 2-5 days. Mean time taken to achieve full feed was 5.30±1.54 days. Time taken to achieve weight of 1600 gm ranged from 6 to 37 days. Maximum number of babies achieved the targeted weight in 8-14 days (32.2%) followed by those who attained this weight within 15-21 days (30%), 22-28 days (21.1%), <7 days (13.3%) and >28 days (3.3%) respectively. Mean time taken to achieve the targeted weight was 16.69±7.19 days (Table 4).

Table 4: Distribution of babies according to time taken to achieve weight of 1600 gm.

Time taken (days)	Group I (n=90)	
	No.	%
≤7 days	12	13.3
8-14 days	29	32.2
15-21 days	27	30.0

To study the weight growth rate study subjects were divided in 4 groups, Group A (weight 1100-1190 gm), Group B (1200-1290 gm) Group C (1300-1390 gm) and Group D (1400-1490 gm). Mean weight growth rate (g/kg/day) was 14.96 g/kg/day in group A, 14.33 g/kg/day in group B, 15.13 g/kg/day in group C and 15.33

g/kg/day in group. Growth rate of weight is shown in Table 5 and 6.

Table 5: Growth rate (g/day) of neonates on HMF.

Weight band	n	Mean	SD
1100-1190 gm	19	17.10	1.87
1200-1290 gm	26	17.78	1.69
1300-1390 gm	22	20.11	2.35
1400-1490 gm	23	21.95	2.36

Table 6: Growth Rate (g/kg/day) of neonates on HMF.

Weight band	n	Mean	SD
1100-1190 gm	19	14.96	1.92
1200-1290 gm	26	14.33	1.64
1300-1390 gm	22	15.13	1.94
1400-1490 gm	23	15.33	1.85
Overall	90	14.91	1.84

DISCUSSION

The present study was carried out over a period of one and half year from January 2015 to June 2016 in the departments of Paediatrics, UP University of Medical Sciences, Saifai, UP, India. In this study a total 92 neonates were analysed. During the recruitment period, inclusion and exclusion criteria were strictly followed. Primarily the purpose of this study was to compare the weight gain of VLBW pre-terms when they were fortified with HMF. Human milk contains numerous immune-protective components that protect the premature infant from sepsis and necrotizing enterocolitis. Because of these protective effects, human milk is the feeding of choice for the premature infant. However, human milk does not provide adequate amounts of most nutrients for premature infants and must therefore be supplemented (fortified) with nutrients.¹¹ With the rapid development of medical technology, the number of premature new borns with small gestational age and low birthweight continues to rise, and clinicians face challenges in providing proper nourishment for these infants. Research has confirmed that breast milk fortifiers can improve short term growth.¹² Commercially available fortifiers provide energy and most nutrients in adequate amounts.¹³ Human milk has the dual functions of supporting and complementing the preterm infant’s developing immune system, and of providing the nutrients needed for growth and development. As a source of nutrients, however, human milk is inadequate, necessitating nutrient supplementation (fortification).¹⁴ There are different methods of fortifying expressed breast milk. When fortifiers were introduced in the 1980s, a substantial number of studies were conducted to assess their effectiveness. Collectively these studies conducted between 1987 and 1999 showed that fortifiers improved growth and various indicators of nutritional status.⁹ Keeping that in mind all the preterm babies in this study were given fortified expressed breast milk with HMF and we didn’t take a control group of unfortified expressed

breast milk only. The aim of fortification is to raise the concentrations of specific nutrients in relation to energy to such levels that nutrient needs are met whenever energy needs are met. Fortification also increases the caloric density of milk, which helps to keep feeding volumes low. Fortifiers achieve this by including carbohydrate(s) and/or lipids.

In present study, on analysis of data, we found that the weight gain of new borns who received HMF fortified maternal milk was 14.91 g/kg/day. Martins EC et al compared the weight and height gain and the frequency of clinical complications in preterm new borns weighing less than 1,500 g, exclusively fed human milk or fortified human milk until reaching 1,800g.¹⁵ Prospective double-blind randomized controlled trial involving 40 preterm infants weighing <1,500 g at birth and ≤34 weeks of gestational age. Daily weight gain, weekly length and head circumference gain, nutritional variables and clinical complications were compared. Human milk fortification resulted in better growth, the weight gain was 24.4 and 21.1 g/day (p = 0.075). There were no significant clinical complications.

Mukhopadhyay K et al studied the effects of human milk fortification on 166 infants (Preterm infants weighing ≤1500 grams and ≤34 weeks of gestation) on short term growth and biochemical parameters in preterm very low birth weight (VLBW) appropriate for gestation (AGA) and small for gestation (SGA) babies.¹⁶ Primary outcome measures were Short-term growth (daily weight, length and head circumference (HC) weekly) till discharge or 2 Kg. Fortification resulted in better growth in preterm VLBW babies as compared to control group. Weight gain (15.1 and 12.9 g/kg/d, P <0.001), length (1.04 and 0.86 cm/week, P = 0.017) and HC (0.83 and 0.75cm/week, P<0.001) increased significantly in fortified group. The results found in the present study are similar to those found in the literature. There is great difficulty in keeping mothers in a hospital setting, with maternal milk available for manual expression during the whole period of hospital stay, and this was only possible in the present study because mothers were offered accommodations during the whole period of study, in addition to nutritional and psychological follow-up provided by the multi-professional and interdisciplinary team. There were few limitations to our study. One of the limitation of our study was small sample size. The small study populations are evidenced by the wide confidence intervals. Such small numbers may not allow high enough power to detect differences in, for example, NEC incidence. A study with larger sample size is needed for further validation of results. A multi centric study with a large sample size will be able to overcome these limitations.

In summary, fortified human milk has tremendous benefits in improving the growth and short term outcomes for the premature infant. Mother's own milk has clear advantages due to its composition. Premature infants need fortification of human milk to achieve

growth as recommended. Based on the results of this study, we concluded that the supplementation with HMF, can result in a significant increase in growth (weight, linear and head growth).

Despite the favorable results regarding the use of HMF, further studies are needed to improve and individualize the nutrition of very low birth weight preterm infants, taking into consideration the composition of maternal milk and each new-born's needs. It is possible that new studies might demonstrate results obtained with the use of fortifiers extracted from human milk.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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