CLINICAL STUDY

Effect of Protein and Energy Supplementation on Growth of Infants ≤1,500 g at Birth: A Randomized Trial

JANARDHAN SHENOY*, NIVETHITHA†, SUCHETHA RAO*

ABSTRACT

Objective: To study the effect of energy supplements with protein-energy supplementations on the growth patterns of low birth weight (LBW) infants weighing ≤1,500 g. **Material and methods:** Babies with birth weight of ≤1,500 g and on full enteral feeds on Day 14 of life with expressed breast milk (n = 60) were randomly allocated to energy alone group (n = 30) and protein-energy group (n = 30). Babies in energy intervention received medium-chain triglyceride and protein-energy intervention received human milk fortifier supplement added to expressed breast milk. Daily weight, weekly length and head circumference were checked to monitor the growth. Study was continued till the infants reached a weight of 1,600 g or 4 weeks from the start of the study, whichever was earlier. **Results:** In the energy group, mean weight gain was 14.98 ± 0.09968 g/kg/day, whereas in the protein-energy group weight gain was 19.79 ± 0.08745 g/kg/day ($p < 0.001$). Increase in length or head circumference did not show any statistical significance. **Conclusion:** This study was consistent with the importance of providing additional protein intake to achieve increased postnatal growth in LBW babies.

Keywords: Low birth weight, feeding, protein-energy supplements

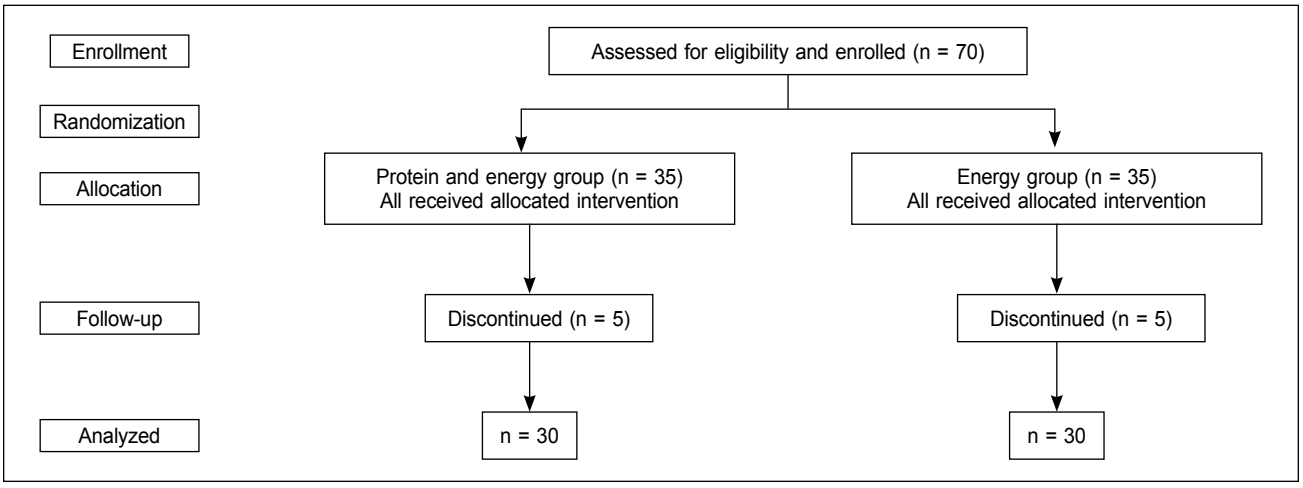
Nutritional management of the very low birth weight (VLBW) infants is quite a challenge for present neonatal intensive care unit (NICU) teams.[1] Most VLBW infants have discharge weight below the 10th percentile of reference intrauterine weights leading to postnatal growth restriction.[2,3] Poor neonatal weight gain and head growth have been linked to significant neurodevelopmental outcomes. Interventions to improve antenatal and postnatal growth may contribute to better school-age outcomes.[4] To achieve the necessary catch-up growth, nutritional supplements have been added to standard preterm formula or fortified human milk.[1] Preterm infants inevitably accumulate a significant nutrient deficit in the first few weeks of life, if fed only with recommended daily allowance of nutrients. This deficit can be directly related to subsequent postnatal growth retardation.[3]

We conducted a randomized controlled trial to study the effect of energy supplements with protein-energy supplementations on the growth patterns of low birth weight (LBW) infants weighing ≤1,500 g.

MATERIAL AND METHODS

It was a prospective, randomized controlled trial done in a tertiary care hospital in Dakshina Kannada district of Karnataka. The study was conducted from March 2011 to July 2012. After getting parental consent, babies with birth weight of ≤1,500 g and on full enteral feeds on Day 14 of life were included in the study. Babies with major congenital malformation, suspected or confirmed necrotizing enterocolitis, requiring major surgery, genetic defects, congenital infection, suspected inborn errors of metabolism and on formula feeding were excluded from the study. Study was conducted after Institutional Ethical Committee clearance. A total of 70 infants were included in the study. Infants were randomly assigned into two groups using randomization table, either protein and energy group or energy alone

*Associate Professor
Dept. of Pediatrics
Kasturba Medical College, Mangalore, Manipal University, Karnataka
†Consultant Pediatrician
Kiruthika Hospital, Tirupur, Tamil Nadu
Address for correspondence
Dr Suchetha Rao
Dept. of Pediatrics
Kasturba Medical College, Attavar, Mangalore - 575 001
Manipal University, Karnataka
E-mail: suchethasr@gmail.com



group. Each group comprised of 35 infants. They were categorized into appropriate-for-gestational age (AGA) or small-for-gestational age (SGA) in each group. Study was continued till the infants reached a weight of 1,600 g or 4 weeks from the start of the study, whichever was earlier. Babies developing any feed intolerance or any other complications were excluded from the study. Five babies from each group were excluded during the course of the study due to feed intolerance and insufficient lactation in the mother. Thirty babies in each group were finally analyzed. Babies were feed through nasogastric tube every 2 hours. Trained nurse fed the babies.

Those babies randomized to the energy-alone intervention received medium-chain triglyceride (MCT). Each milliliter of MCT oil was added to 50 mL of expressed breast milk (EBM). Those babies randomized to protein-energy intervention received human milk fortifier (HMF). One sachet of 2 g of HMF was added to 50 mL of expressed milk. All babies receiving protein-energy and energy alone supplement had received only mother's milk. Protein and calorie content per 100 mL of breast milk given to each group is shown in Table 1.

Babies were managed in the same postnatal ward with same ambient temperature. Babies of both groups were provided with cap, gloves, socks and they were rapped with cotton sheet and covered with blankets to prevent the heat loss.

Growth rate was measured during the study period by:

- Daily weights by electronic weighing machine (Jee-lit with an error of 10 g). The weight was recorded at the same time of the day in all babies.
- Weekly length by infantometer
- Weekly head circumference by nonstretchable inch/centimeter tape.

Table 1. Comparison of Caloric and Protein Content of Breast Milk With and Without Nutritional Supplements

	Calories (kcal) per 100 mL	Protein (g) per 100 mL
Human milk	68	1.1
Human milk + MCT	83.4	1.1
Human milk + HMF	82.94	1.5

Mean weight gain in grams per kg per day was calculated by subtracting first day weight from last day weight and dividing it by total number of days and birth weight.

RESULTS

Thirty-five babies were included to energy alone group and 35 babies to energy and protein group in the beginning of the study. Five babies from each group were excluded during the course of the study due to feed intolerance and insufficient lactation in the mother. Thirty babies in each group were finally analyzed. Birth weight, gestational age, gender and other baseline characteristics did not differ significantly between two groups (Table 2).

There was no significant difference in weight gain between male and female babies in this study. The weight gain in the infants receiving protein-energy supplementation was significantly better than those receiving energy alone group (Table 3). In the energy group, mean weight gain was 14.98 ± 0.09968 g/kg/day, whereas in the protein-energy group weight gain was 19.79 ± 0.08745 g/kg/day ($p < 0.001$). The infants randomized to protein-energy group regained the birth weight and target weight faster than energy alone group but this was not statistically significant. Energy

Table 2. Baseline Characteristics of Each Group

Variables	Energy alone group (MCT) (n = 30)	Protein and energy group (HMF) (n = 30)	P value
Mean birth weight (grams)	1.26	1.19	0.678
Mean gestational age (weeks)	32.94	32.5	0.996
SGA	18 (60%)	17 (57%)	0.943
Gender (males)	16 (53%)	18 (60%)	0.865

Table 3. Outcome of Nutritional Intervention

Parameters	Energy alone group (MCT) (n = 30) mean ± SD	Protein and energy group (HMF) (n = 30) mean ± SD	P value
Weight gain (g/kg/day)	14.98 ± 0.09968	19.79 ± 0.08745	< 0.001
Length gain (cm/week)	0.375 ± 0.09167	0.402 ± 0.08461	0.632
Head circumference (cm/week)	0.395 ± 0.09534	0.414 ± 0.08567	0.783
Number of days to regain birth weight	8 ± 2.598	4.2 ± 2.856	0.15
Duration of study	25.6 ± 3.67157	21 ± 2.74159	0.19

alone group attained birth weight and target weight in 8 ± 2.598 days and in 25.6 ± 3.6715 days, respectively.

Protein-energy group attained birth weight and target weight in 4.4 ± 2.856 days and 21 ± 2.74159 days, respectively. SGA babies gained target weight faster than AGA but without statistical significance. There is no significant difference in weight loss in two groups before including into the study. Head circumference increased by 0.395 cm/week in energy alone group and 0.414 cm/week in protein-energy alone group. Length increased by 0.375 cm/week in energy alone group and 0.402 cm in protein-energy alone group. Increase in length or head circumference did not show any statistical significance.

DISCUSSION

LBW infant's adaptation to extrauterine life is an energy consumptive process.[5] Postnatal growth retardation is a major issue in preterm infants.[6] Optimizing growth in the preterm infant continues to be a difficult task and is complicated by a lack of knowledge of the optimal growth pattern. Adequate postnatal growth is necessary for optimal neurological outcome. Prevention of postnatal growth failure requires a comprehensive nutritional regimen that provides adequate nutritional support as soon after birth as possible and is maintained throughout an infant's hospital course.[7] The general trend in many of the NICU in the developing countries to increase the postnatal growth of LBW babies is by addition of MCT oil. HMF is not widely used. Addition of HMF will provide energy as well as protein to the growing babies, but MCTs will provide energy alone. Hence, this study was done to compare the effectiveness of protein-energy supplement over energy supplement.

Brumberg et al[1] compared the growth in the babies, those received energy alone with those who received protein and energy supplements. The babies in the energy alone gained 11.5 ± 4.8 g/kg/day and protein-energy group babies gained 17 ± 2.4 g/kg/day.[1] In the present study, babies in the energy alone group gained 14.98 ± 0.09968 g/kg/day and those in protein-energy group gained 19.79 ± 0.08745 g/kg/day.

Gathwala et al[8] studied the effect of HMF supplements in SGA babies. The babies who received fortified milk gained a mean weight of 38.77 ± 7.43 g/day, which was significantly better than expressed milk alone group babies who gained 28.71 ± 3.18 g/day. The present study included both SGA and AGA babies. Mukhopadhyay et al[9] showed that when preterm babies were fed fortified human milk they had better growth and they compared them with mineral supplements. They followed the babies till they reached 2 kg, whereas in our study we followed them till 1.6 kg. On subgroup analysis, they found that SGA preterm babies fed with fortified milk had significantly better growth than those fed unfortified milk as compared to AGA babies. Our study also shows that SGA babies gained faster than the AGA babies but statistically it was not significant. The mean birth weight of the LBW babies in their study was 1.2 kg, which was similar to our study.

Study by Miller et al[10] showed that increasing the protein content of HMF improved the growth of LBW babies of <31 weeks gestation. Lucas et al[11] showed that developmental scores at 18 months were slightly but not significantly better in the preterm who received protein supplements. Present study has limitation that follow-up was not done.

CONCLUSION

Present study highlights the continued need of enteral protein in growth of VLBW infants. To improve growth in these infants, supplementation of EBM with protein must be considered. This study has shown the growth benefits of increasing caloric intake with a multinutrient supplement that provides both protein and energy compared with a supplement that provides only energy.

REFERENCES

1. Brumberg HL, Kowalski L, Troxell-Dorgan A, Gettner P, Konstantino M, Poulsen JF, et al. Randomized trial of enteral protein and energy supplementation in infants less than or equal to 1250 g at birth. J Perinatol. 2010;30(8): 517-21.
2. Cooke RJ, Ainsworth SB, Fenton AC. Postnatal growth retardation: a universal problem in preterm infants. Arch Dis Child Fetal Neonatal Ed. 2004;89(5):F428-30.
3. Embleton NE, Pang N, Cooke RJ. Postnatal malnutrition and growth retardation: an inevitable consequence of current recommendations in preterm infants? Pediatrics. 2001;107(2):270-3.
4. Peterson J, Taylor HG, Minich N, Klein N, Hack M. Subnormal head circumference in very low birth weight children: neonatal correlates and school-age consequences. Early Hum Dev. 2006;82(5):325-34.
5. Ernst KD, Radmacher PG, Rafail ST, Adamkin DH. Postnatal malnutrition of extremely low birth-weight infants with catch-up growth postdischarge. J Perinatol. 2003;23(6):477-82.
6. Cooke R. Postnatal growth in preterm infants: have we got it right? J Perinatol. 2005;25 Suppl 2:S12-4.
7. Uhing MR, Das UG. Optimizing growth in the preterm infant. Clin Perinatol. 2009;36(1):165-76.
8. Gathwala G, Chawla M, Gehlaut VS. Fortified human milk in the small for gestational age neonate. Indian J Pediatr. 2007;74(9):815-8.
9. Mukhopadhyay K, Narnag A, Mahajan R. Effect of human milk fortification in appropriate for gestation and small for gestation preterm babies: a randomized controlled trial. Indian Pediatr. 2007;44(4):286-90.
10. Miller J, Makrides M, Gibson RA, McPhee AJ, Stanford TE, Morris S, et al. Effect of increasing protein content of human milk fortifier on growth in preterm infants born at <31 wk gestation: a randomized controlled trial. Am J Clin Nutr. 2012;95(3):648-55.
11. Lucas A, Fewtrell MS, Morley R, Lucas PJ, Baker BA, Lister G, et al. Randomized outcome trial of human milk fortification and developmental outcome in preterm infants. Am J Clin Nutr. 1996;64(2):142-51.