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THE EFFECT OF ORAL PROTEIN SUPPLEMENTATION ON THE GROWTH OF VERY LOW BIRTH WEIGHT PRETERM INFANTS ADMITTED TO THE NEONATAL INTENSIVE CARE UNIT: A RANDOMIZED CLINICAL TRIAL

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Abstract

Background: *During NICU admission, extra-uterine growth retardation that can affect the neurodevelopmental outcome is a challenging problem in extremely preterm infants. This trial aimed to determine the effect of additional enteral protein supplementation on the growth velocity of the anthropometric parameters.*
Method: *In this randomized controlled trial, 77 preterm infants (gestational age ≤33 weeks and birth weight <1500 g) who reached full enteral feeding with either fortified breast milk or preterm formula were included. They were randomized to receive either 4-<5 g/kg/day protein through extra protein supplementation (intervention) or 3-<4 g/kg/day protein. Weight gain, as well as length and head circumference growth, were monitored daily and weekly, respectively. Venous blood gas, blood urea nitrogen (BUN), and albumin levels were checked weekly.*
Results: *Five out of 77 participants were excluded due to feeding intolerance. Analyses were conducted on 36 neonates with protein intake of 3.66 ± 0.22 gr/kg/day and 36 with extra protein intake. Baseline characteristics were similar between the groups. An additional protein supply of 0.89 gr/kg/day, resulting in an average protein intake of 4.55 ± 0.18 in the intervention group, increased the postnatal weight gain, linear growth, and head circumference growth (7.98 gr/kg/day, 0.347 cm/week, and 0.38 cm/week, respectively). The albumin levels were significantly increased, but the BUN levels were not significantly increased in the intervention group. None of the patients developed necrotizing enterocolitis or significant acidosis.*
Conclusion: *Protein supplementation significantly improves the growth of the anthropometric parameters. An increase in serum albumin and no increase in serum urea can indicate the anabolic effect of extra protein. Protein supplementation can add to routine feeding protocols of VLBW infants without any short-term adverse effect; however, further study for evaluation of long-term complications is needed.*

Keywords

Protein supplement, Preterm infants, Growth, Nutrition, VLBW

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Introduction

The last trimester of pregnancy, which is often lost in preterm birth, is the time when the fetus has the most protein intake for growth. Furthermore, extremely preterm infants lose protein approximately twofold that of term infants [1]. Therefore, preterm newborns often experience a negative nitrogen balance. Prematurity is a nutritional emergency since studies demonstrate that these infants experience extra-uterine growth retardation as a result of a cumulative deficiency in

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albumin levels which were significantly higher in the protein supplement group and increased significantly in this group throughout the study (based on repeated measures analysis). In the Cochrane review published at 2020 [24] which evaluated high versus low protein intake in the formula-fed LBW infants, no study addressed serum albumin as a secondary outcome; however, in studies which compared very high versus low protein intake, Cooke et al. [25] reported serum albumin levels and found no significant differences between the two groups. Van der Aker et al. reported that albumin synthesis was stimulated by parenterally administrated amino acid in preterm infants [26]. The increase in serum albumin in our neonates can indicate the anabolic effect of extra protein and increased weight gain velocity is due to protein and fat accretion. One putative risk for high protein intake is increased concentrations of hydrogen ions as a result of the immaturity of amino acid metabolic pathways in preterm infants [27], and metabolic acidosis may develop. Hence, we evaluated the acid-base status of the participants. The PH was significantly lower, while PCO2 and HCO3 were higher in the protein group than the controls (after intervention). Based on repeated measures analysis, however, the changes in the PH level and HCO3 levels were not statistically significant throughout the study in both groups. Thus, no significant metabolic acidosis developed, like the result of Cooke et al.'s study [25].

Our study had some limitations such as a lack of long-term follow-up of our patients and the small sample size. However, based on group matchings and insignificant differences between the baseline features of our groups, we believe that our study could provide insight into further multicentral RCTs and review of articles to obtain the most satisfactory treatment and supplement regimen for neonates.

Conclusion

Protein supplement significantly improved the growth of all aspects of the anthropometric parameters including weight, length, and head circumference. No short-term adverse effect was detected during the study. This study could provide insight into further multicenter RCTs to define the optimal levels of protein intake for VLBW neonates and add protein supplement to the routine feeding protocols. Furthermore, long-term studies are needed to evaluate long-term benefits, especially on neurodevelopment and probable complications of this intervention.

Conflicts of interest

No conflicts of interest were declared by the authors.

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Abbreviations

GA: Gestational Age
BUN: Blood Urea Nitrogen
VLBW: Very Low Birth Weight
NEC: Necrotizing Enterocolities
SGA: Small for Gestational Age
HC: Head Circumference
FBM: Fortified Breast Milk
PF: Premature Formula
PNGF: Post Natal Growth Failure
NICDH: National Institute of Child Health and Human Development
PDA: Patent Ductus Arteriosus
MOM: Mothers' Own Milk
AAP: American Academy of Pediatrics
ESPGHAN: European Society for Pediatric Gastroenterology Hepatology and Nutrition

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