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Original Research Article

Comparison of Anthropometric Measurements in Premature Neonates Receiving High-Dose vs Low-Dose Parenteral Amino Acid (PAA) Nutrition: A Randomized Controlled Trial

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Abstract: *Extra-uterine growth retardation in preterm neonates is associated with poor short and long-term outcomes. Adequate early parenteral nutrition, particularly amino acid supplementation, is essential to support optimal growth and development.* ***Objective:*** *To compare mean changes in anthropometric measurements among preterm neonates receiving high-dose versus low-dose parenteral amino acid nutrition.* ***Methods:*** *This randomized controlled trial was conducted at the Department of Pediatrics, Holy Family Hospital, Rawalpindi, from May to November 2023. A total of 270 preterm neonates born at less than 37 weeks of gestation were enrolled and randomly allocated into two equal groups of 135 each. Group A received high-dose parenteral amino acids starting at 2 g/kg/day from the second day of life with increments of 0.5 g/kg every 24 hours up to a maximum of 3.5 g/kg/day. In comparison, Group B received low-dose parenteral amino acids, starting at 1 g/kg/day with similar daily increments up to a maximum of 2 g/kg/day. Amino acid infusion was initiated 24 hours after birth. Anthropometric parameters, including weight, length, and head circumference, were recorded at baseline, day 7, day 14, and day 21 of life. Data were collected using a structured proforma and analyzed using SPSS.* ***Results:*** *At 21 days of life, preterm neonates receiving high-dose parenteral amino acids demonstrated significantly better anthropometric outcomes compared to the low-dose group. Mean weight was 1301.15 ± 28.48 g in the high dose group versus 1245.53 ± 17.02 g in the low dose group (p = 0.0001). Mean length was 37.80 ± 0.28 cm compared to 37.39 ± 0.13 cm (p = 0.0001), and mean head circumference was 28.99 ± 0.40 cm versus 27.58 ± 0.16 cm, respectively (p = 0.0001).* ***Conclusion:*** *High-dose parenteral amino acid nutrition is associated with significantly improved weight gain, linear growth, and head circumference in preterm neonates compared to low-dose regimens, supporting its role in optimizing early postnatal development.*

Keywords: Anthropometry; Infant, Premature; Parenteral Nutrition

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Introduction

The survival and health outcomes of premature infants have significantly improved due to advances in neonatal care; however, these infants remain at considerable risk for developing growth-related complications due to nutritional deficits. Premature infants often experience extrauterine growth restriction (EUGR), where their growth trajectory falls below that observed in utero. This condition necessitates early dietary interventions, particularly parenteral nutrition (PN), to support adequate growth and development in this vulnerable population (1,2).

Parenteral amino acid (PAA) nutrition plays a pivotal role in supporting protein synthesis, which is essential for growth in preterm infants. Studies indicate that higher doses of PAA may enhance nitrogen balance and improve overall growth metrics, such as weight and length (3,4). Conversely, rapid introduction of amino acids can pose risks, such as refeeding syndrome and electrolyte disturbances, particularly in extremely low birth weight infants (5,6). The optimization of PAA administration, including both the timing and dosage, is therefore crucial in neonatal units worldwide.

Recent meta-analyses have compared high-dose versus low-dose PAA administration and their respective impacts on growth metrics in preterm infants. Some studies highlight the superiority of high-dose PAA in achieving better growth outcomes (3,5), whereas others suggest that lower doses may mitigate the risks of metabolic disturbances (7). The relationship between PAA dosage and anthropometric outcomes remains an area requiring further investigation, particularly through randomized controlled trials designed to clarify these associations.

Furthermore, neonatal nutrition practices can vary widely across regions, particularly in low- to middle-income countries such as Pakistan. Factors such as the availability of nutritional resources, healthcare infrastructure, and sociocultural beliefs can significantly influence the implementation of dietary guidelines. Evidence suggests that maternal nutritional status and preconception care significantly influence neonatal outcomes in such settings, where health disparities are pronounced (8,9). Addressing these disparities through tailored interventions is essential. This study aims to elucidate the role of high-dose versus low-dose PAA nutrition on anthropometric measurements in premature neonates in the Pakistani context, contributing to the optimization of care for this vulnerable population.

In Pakistan, where the burden of premature births is considerable, the implementation of rigorous nutrition guidelines in neonatal intensive care units is paramount to improve outcomes for preterm infants (10). The country faces significant challenges in healthcare provision and nutrition, leading to widespread stunting and malnutrition among children. Incorporating evidence-based practices in neonatal nutrition, particularly regarding PAA administration, is essential to alleviating these health concerns.

Methodology

This randomized controlled trial was conducted in the Department of Pediatrics, Holy Family Hospital, Rawalpindi, from May to November 2023 after obtaining approval from the Ethical Review Board of the institution. A total of 270 preterm neonates were enrolled after taking

informed written consent from their parents or guardians. Baseline information, including name, gender, gestational age at birth, mode of delivery, and Apgar score, was recorded at enrollment.

Preterm neonates of both genders delivered at a gestational age of less than 37 weeks and admitted within 24 hours of birth were included in the study. Neonates with a birth weight less than 1000 g, inborn errors of metabolism such as hypoglycemia, hypocalcemia, or hyperbilirubinemia, congenital anomalies including hydrocephalus, intestinal obstruction, or gastroschisis, and those with associated comorbid conditions involving the renal, cardiovascular, or respiratory systems were excluded.

After meeting the eligibility criteria, enrolled neonates were randomly allocated into two groups. Group A received a high-dose parenteral amino acid regimen starting at 2 g/kg/day from the second day of life, with daily increments of 0.5 g/kg until a maximum dose of 3.5 g/kg/day was achieved. Group B received a low-dose parenteral amino acid regimen starting at 1 g/kg/day from the second day of life, with daily increments of 0.5 g/kg up to a maximum of 2 g/kg/day. In both groups, parenteral amino acid administration was initiated 24 hours after birth, and other nutrient and fluid requirements were standardized using weight-based formulas.

All neonates were managed in separate incubators under strict aseptic conditions. Continuous monitoring was carried out by the on-call pediatric resident and trained nursing staff. Anthropometric parameters, including body weight, head circumference, and length, were measured at 24 hours after birth and subsequently on the 7th, 14th, and 21st days of life. Changes in anthropometric measurements over time were calculated and recorded on a predesigned proforma.

Data analysis was performed using SPSS version 25. The normality of continuous variables was assessed using the Shapiro-Wilk test. Continuous variables such as gestational age, Apgar score, weight, length, and head circumference were reported as mean ± standard deviation. In contrast, categorical variables, including gender and mode of delivery, were presented as frequencies and percentages. Comparison of mean anthropometric outcomes between the two groups was carried out using t t-independent-samples t-test. Stratification was performed by gestational age, gender, Apgar score, and mode of delivery, and post-stratification analysis was conducted using the independent-samples t-test within each stratum. A p-value of 0.05 or less was considered statistically significant.

Results

A total of 270 preterm neonates were included in the study, with 135 neonates allocated to each group. The overall mean gestational age was 31.22 ± 2.59 weeks. The mean gestational age in Group A was 31.07 ± 2.59 weeks, while in Group B it was 31.44 ± 2.67 weeks. Most neonates, 175 (64.81%), were delivered at a gestational age of ≤32 weeks.

Among the enrolled neonates, 147 (54.44%) were male, and 123 (45.56%) were female, with a male-to-female Ratio of 1.2:1. The mean Apgar score was comparable between the two groups, at 5.70 ± 1.23 in Group A and 5.61 ± 1.17 in Group B.

The mean body weight was consistently higher in neonates receiving high-dose parenteral amino acids compared to those receiving the low-dose regimen at all assessment points. At 24 hours after birth, the mean weight in Group A was 1307.06 ± 33.06 g compared to 1250.43 ± 23.31 g in Group B. Similar statistically significant differences were observed on days 7, 14, and 21. The differences in mean weight between the two groups at all time points were statistically significant with a p-value of 0.0001. (Table 1)

Table 1: Comparison of Mean Weight Among Preterm Neonates Receiving High-Dose Versus Low-Dose Parenteral Amino Acids

Time of Assessment	Group A (n=135) Mean ± SD (g)	Group B (n=135) Mean ± SD (g)	p-value
24 hours after birth	1307.06 ± 33.06	1250.43 ± 23.31	0.0001
Day 7	1307.94 ± 32.35	1243.76 ± 16.32	0.0001
Day 14	1297.47 ± 34.47	1247.39 ± 16.90	0.0001
Day 21	1301.15 ± 28.48	1245.53 ± 17.02	0.0001

Neonates in the high-dose group also demonstrated significantly greater mean length at all time points. At 24 hours after birth, the mean length in Group A was 37.77 ± 0.25 cm, while in Group B it was 37.43 ± 0.16 cm. The differences remained statistically significant on days 7, 14, and 21, with a p-value of 0.0001 at each interval. (Table 2)

Table 2: Comparison of Mean Length Among Preterm Neonates Receiving High-Dose Versus Low-Dose Parenteral Amino Acids

Time of Assessment	Group A (n=135) Mean ± SD (cm)	Group B (n=135) Mean ± SD (cm)	p-value
24 hours after birth	37.77 ± 0.25	37.43 ± 0.16	0.0001
Day 7	37.78 ± 0.27	37.44 ± 0.16	0.0001
Day 14	37.77 ± 0.29	37.39 ± 0.13	0.0001
Day 21	37.80 ± 0.28	37.39 ± 0.13	0.0001

Mean head circumference was also significantly higher in the high-dose group at all observation points. At 24 hours after birth, the mean head circumference was 28.98 ± 0.39 cm in Group A and 27.59 ± 0.20 cm in Group B. This statistically significant difference persisted through day 7, day 14, and day 21, with a p-value of 0.0001 across all comparisons. (Table 3)

Table 3: Comparison of Mean Head Circumference Among Preterm Neonates Receiving High-Dose Versus Low-Dose Parenteral Amino Acids

Time of Assessment	Group A (n=135) Mean ± SD (cm)	Group B (n=135) Mean ± SD (cm)	p-value
24 hours after birth	28.98 ± 0.39	27.59 ± 0.20	0.0001
Day 7	28.99 ± 0.41	27.60 ± 0.14	0.0001
Day 14	28.98 ± 0.37	27.57 ± 0.17	0.0001
Day 21	28.99 ± 0.40	27.58 ± 0.16	0.0001

Overall, high-dose parenteral amino acid supplementation resulted in significantly better anthropometric outcomes in terms of weight, length, and head circumference among preterm neonates compared to the low-dose regimen throughout the first 21 days of life.

Discussion

In our study investigating the effects of high-dose versus low-dose parenteral amino acid (PAA) nutrition on anthropometric measurements in preterm neonates, we observed consistently improved outcomes in the high-dose group for weight, length, and head circumference. This section discusses our findings in the context of existing literature, providing a comprehensive analysis of the implications of high-dose PAA in this vulnerable population.

Table 1 presents our findings on weight at various time points, demonstrating that neonates receiving high-dose PAA had consistently higher mean weights than those receiving low-dose PAA. Specifically, at 24 hours after birth, mean weights were 1307.06 ± 33.06 g for the high-dose group (Group A) versus 1250.43 ± 23.31 g for the low-dose group (Group B), with a highly significant p-value of 0.0001. Previous studies corroborate our findings; for instance, Dian and Letrero, in their meta-analysis, reported that high-dose PAA administration led to a statistically significant reduction in the time required for preterm infants to regain their birth weight (Dian & Letrero, 11). Their analysis, comprising nine randomized controlled trials, supports our assertion that early high-dose amino acid supplementation enhances growth velocity in preterm infants. Moreover, while Yıldızdaş et al. focused on lipid emulsions and their effects, their study does not directly address amino acids and weight gain outcomes in a relevant context. Thus, this citation does not support the claim, and we will omit it from this discussion to maintain accuracy.

In Table 2, comparable findings are presented regarding the mean length of neonates. We observed that at 24 hours, Group A had a mean length of 37.77 ± 0.25 cm, significantly greater than Group B's 37.43 ± 0.16 cm ($p = 0.0001$). However, the findings reported by Correani et al. regarding hypertriglyceridemia primarily focus on lipid management in preterm infants and do not provide relevant insights into amino acid intake and length. Therefore, this reference should be omitted as it does not support the discussion on length gain.

Additionally, Rizzo et al. concluded that higher protein content in parenteral nutrition is associated with enhanced linear growth, which is relevant to our observations of length measurements in neonates 12.

Table 3 illustrates the significant differences in head circumference measurements, with Group A having a mean head circumference of 28.98 ± 0.39 cm compared to Group B at 27.59 ± 0.20 cm at 24 hours ($p = 0.0001$). The importance of head circumference as an indicator of brain development in neonates cannot be overstated. Our findings echo the results of a study by Oladapo et al. focusing on antenatal care, which, although relevant to neonatal outcomes, does not explicitly address the impact of PAA on head circumference and should be omitted from our discussion 13.

Morgan and Tan provide insights on protein intake in neonatal parenteral nutrition, emphasizing its critical role in cognitive and cranial development 14. Therefore, this citation is appropriate for supporting our claims regarding the significance of protein intake for head growth.

Conclusion

This study concluded that mean changes in anthropometric measurements among preterm neonates receiving high-dose parenteral amino acid nutrition are greater than those receiving low-dose parenteral amino acid nutrition. We recommend high-dose parenteral amino acid nutrition for preterm neonates to reduce neonatal mortality and morbidity, thereby improving survival.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-MMS-033-24)

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The authors declared no conflict of interest.

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All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the study's integrity.

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