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Original article

Parenteral nutrition using corrected weight to the 10th percentile improves weight gain in preterm neonates: A randomized controlled trial

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SUMMARY

Background: Parenteral nutrition (PN) plays a crucial role in providing nutritional support to premature and small for gestational age (SGA) neonates. In this randomized controlled study, we evaluated PN administration in preterm SGA neonates using the corrected weight estimated at the 10th percentile, as guided by a clinical decision support system (CDSS).

Methods: A total of 100 SGA neonates were randomly assigned to either the Control group (n = 50) or the Intervention group (n = 50). Both groups received PN support using a specialized CDSS. In the Control group, the CDSS calculated the PN regimen based on the actual birth weight, whereas in the Intervention group, calculations were based on the corrected weight corresponding to the 10th percentile. Growth indicators (i.e., body weight, length, and head circumference) were measured at baseline and at the time of exclusive enteral feeding initiation (endpoint).

Results: At baseline, no differences were observed between the two groups regarding gestational age, sex, birth weight, length, level of prematurity (all p's > 0.05). At the endpoint, the median weight gain was greater in the intervention group (+0.16 kg) than that of the control group (+0.09 kg), p = 0.034. The relative change in body weight was higher in the intervention group (+13.6 %) compared to the control group (+6.4 %), p = 0.047.

Conclusions: Nutrient estimation based on the 10th percentile of weight with the assistance of CDSS, appears to be the most favorable combination for faster weight gain among SGA neonates.

Trial Registration: ClinicalTrials.gov NCT07236957.

1. Introduction

Nutritional management is an important component of clinical decision-making in the Neonatal Intensive Care Unit (NICU), especially for neonates at high risk of postnatal grow. Despite advances in the NICU that have improved survival rates, many low birth weight-infants leave the NICU with poor postnatal growth [1]. When enteral feeding is not possible or insufficient, parenteral nutrition (PN) becomes essential for newborns as an intervention not only for metabolic stability but also for postnatal growth [2–4].

Small for gestational age (SGA) infants, a particularly vulnerable population in the NICU, face a lot of issues regarding nutritional support [5]. SGA refers to neonates whose birth weight is below the 10th percentile for their gestational age [6] and without proper interventions, they face a heightened risk of significant growth deficiencies and developmental impairments [7]. Moreover, SGA newborns are more prone to perinatal morbidity and mortality than normal gestational age infants [8]. Insufficient nutrient intake after birth can significantly affect growth. The nutritional challenges, for very low or low birth weight SGA infants, become more intense, particularly as their energy and nutrient needs increase with decreasing gestational age and birth

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weight [9]. In addition, factors such as maternal health, environmental exposures, and congenital conditions contribute to the multifaceted nature of their nutritional needs [10,11].

In clinical practice, PN prescription is ideally based on individualized nutritional requirements. However, to administrate the PN multiple steps are involved, including prescription, calculation and formulation constraints. As a result, discrepancies between the ideal and delivered PN may occur, potentially affecting nutritional adequacy in high-risk populations such as SGA neonates [12,13]. Given the complexity of PN prescription and the need for precise nutrient estimation in SGA neonates, clinical decision support systems (CDSS) have been increasingly used to support clinical decision-making in the NICU [14,15]. These systems are designed to customize the macronutrient and micronutrient prescriptions by tailoring nutrition plans to each individual's specific needs. Determining the proper energy intake is essential in PN, as both undernutrition and overfeeding can adversely impact an infant's growth and overall health [16]. It is suggested that CDSS tools help healthcare providers and clinicians make more accurate decisions regarding nutrient administration [15]. This individualized approach is particularly important for newborns with higher energy and nutrient requirements, ensuring that they receive the precise nutritional support they need to grow at an optimal rate.

Given the importance of providing proper nutritional regimens and guidelines to SGA infants, the aim of the present work was to assess infant growth (i.e., body weight, length, and head circumference) when energy and nutrient estimations were based on actual birth weight vs. the corrected weight (adjusted to the 10th percentile of growth curves), with the assistance of specialized CDSS.

2. Materials and methods

2.1. Study design

In the present parallel group, single centered trial, a computer-generated simple randomisation sequence was implemented. The study coordinator recorded the code number along with the type of treatment for each participant and sealed data into an envelope. Allocation to treatment was blinded to the care providers and the data scientist until the assessment of study results.

Infants who satisfied the criteria for SGA neonates [17] were assigned to either the Control group or the Intervention group. Both groups received PN support initiated within the first 24 h of life in all newborns. In the control group, PN regimen was based on the actual birth weight, whereas in the intervention group, calculations were based on the corrected weight corresponding to the 10th percentile for SGA neonates [17], as described in the "Measurements" section. The duration of the intervention was not predetermined; instead, the duration of PN was treated as an outcome measure, as described in the "*Primary outcome and sample size calculation*" section below.

In both groups, PN was calculated and prescribed using a specialized CDSS [15,18]. This CDSS incorporated therapeutic and pharmaceutical protocols approved by the hospital's scientific committee, and was developed through a comprehensive literature review and the clinical expertise of neonatologists and specialized nutrition pharmacists [15,18].

2.2. Participants

A sample size of 100 premature SGA neonates was included in the study. All SGA neonates were hospitalized at the IASO Hospital in Athens, Greece. Before the commencement of the recruitment process, the parents signed a written informed consent. All eligible volunteers were recruited between the years 2020 and 2023.

2.3. Inclusion and exclusion criteria

Newborns hospitalized in NICU and meeting the criteria for SGA infants, i.e., neonates with birth weight under the 10th percentile [17,19], were included in the study. Additionally, preterm infants receiving exclusive PN as prescribed by one or more physicians were included. Term birth newborns, or newborns not fulfilling the criteria for SGA infants were excluded. Additional exclusion criteria were newborns with primary liver/bile duct disease, and/or newborns receiving enteral nutrition. Neonates whose parents/guardians did not give written consent to participate in the study were excluded.

2.4. Ethics

The Ethics Committee of IASO HOSPITAL in Athens, Greece, examined and approved the study (Approval Code 21-11-18AB). The trial was executed in accordance with the principles of the Helsinki Declaration and adhered to the standards of Good Clinical Practice. ClinicalTrials.gov registry identifier: NCT07236957.

2.5. Measurements

Data on gestational age (weeks), sex (male/female) and growth (i.e., body weight, length and head circumference) were used in the present work.

2.5.1. Anthropometry

Measurements were performed at the baseline (i.e., first day of PN), and on the last day of PN. An electronic scale was employed to retrieve the body weight. The neonates were placed, twice, at the center of the scale without any clothes and two measurements were obtained [20]. The measurement of body weight was conducted with a precision of one gram. Length was measured using two persons, a high-precision stadiometer and a measuring board including a head and a foot piece. The neonates were placed in a supine position, with shoulders and hips being in contact and the head touching the head piece, while the neonates' legs were pulled straight and the foot piece being pressed against the heel [20]. The measurement of length was obtained with a precision of one millimeter. Head circumference was measured with a non-stretch tape to the nearest 0.1 cm. All anthropometric measurements were performed by two trained assessors following standardized protocols. Additionally, the duration of PN support and the overall number of hospitalization days were documented.

2.5.2. Calculation of the caloric requirements and adequate coverage of PN

The specific CDSS evaluated the caloric requirements for each SGA neonate, as previously described [15]. In brief, the system evaluates input data (anthropometric data, comorbidities, clinical status, specific treatment information), determines nutritional parameters using evidence-based statistical models, and calculates individual daily nutritional requirements for energy, protein, carbohydrates, fats, vitamins, and minerals, as well as the concentration of each nutrient and daily parenteral nutrition volume, based on the updated American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines 2023 [21]. In the present study, the CDSS was programmed to use the birth weight for calculations of caloric and macronutrient requirements for the control group, whereas for the intervention group, the CDSS applied the adjusted weight

corresponding to the 10th percentile for SGA neonates [17]. The specific CDSS was developed using a client–server architecture implemented in C# on the Microsoft.NET Framework 4.8, using Visual Studio 2019 and SQL Server 2019. This CDSS has been previously applied in clinical settings, demonstrating very good adherence to PN guidelines and clinical outcomes [15,22]. The system incorporates an extensive library of age-specific PN protocols applicable to neonates, infants, children, adolescents and adults [15]. Briefly, the system uses evidence-based statistical models to determine nutritional parameters, evaluates input data (anthropometric data, comorbidities, clinical status, and specific treatment information), and computes individual daily nutritional requirements for energy, macronutrients, vitamins, and minerals, as well as the concentration of each nutrient and daily PN volume, all in accordance with ASPEN guidelines [21]. PN composition regarding micronutrients (i.e., minerals, trace elements, vitamins) was calculated with the birth weight for both groups, to avoid electrolyte imbalances and organ dysfunction. For both groups, the CDSS calculated fluid volume based on birth weight, postnatal day, clinical condition and osmolar load, following the ASPEN guidelines [21].

2.5.3. Blood analyses

Blood samples were obtained at the last day of PN, after PN was ceased for 4 h and before oral feeding initiation. To assess the safety and adequacy of the prescribed parenteral nutrition (PN), serum electrolytes (sodium, potassium and calcium), albumin, and haematological parameters—including red blood cell count (RBC), white blood cell count (WBC) and haematocrit (Hct)—were measured as part of the hospital's routine laboratory analyses. Electrolytes (sodium, potassium and calcium) reflect growth outcomes and safety, albumin is a useful marker of nutritional and protein status, while hematological parameters can monitor clinical stability during the PN [23].

Whole blood samples were allowed to clot at room temperature to isolate sera. Blood collection tubes containing ethylenediamine tetraacetic acid (EDTA) were used for plasma separation. Centrifugation was set at 3000 rpm for 10 min at 4 C. Freshly isolated plasma or serum samples were used for all analyses. A biochemical analyzer (Cobas 8000 modular analyser, Roche Diagnostics GmbH, Mannheim, Germany) was used to determine electrolytes and albumin concentrations. Hematology analysis was performed using an automatic analyser (DxH 800 analyser, Beckman Coulter Inc., Nyon, Switzerland).

2.6. Primary outcome and sample size calculation

The primary outcome of the present study was body weight gain during PN. Secondary outcomes included additional indicators of infant growth, namely length and head circumference, as well as the duration of PN. The intervention period was defined as the interval from the first day of PN (baseline) to the final day of PN, thereby corresponding to the duration of intravenous feeding.The sample size was calculated based on the main outcome of weight gain throughout PN intervention.

A minimum sample size of 76 neonates (38 per group) was deemed sufficient to detect a clinically important difference of 3 g/kg/day in weight gain (Standard Deviation = 4) between the control and the intervention group. The calculation was based using a two-tailed t-test with 90 % power and 5 % level of significance.

2.7. Statistical analysis

The categorical variables were presented as counts (n) and percentages (%), while the continuous variables as mean and standard deviations for normally distributed variables or as median and interquartile ranges for skewed variables. The Shapiro–Wilks test was used to identify normality. Student t-test or Mann–Whitney U test, for normally distributed or skewed variables, respectively, were used to identify differences between the two groups. The chi-square test was used to identify differences between the two groups for categorical variables. To investigate possible intra-group differences, paired samples t-test or the Wilcoxon test was applied. Statistical significance was set-up at p-value <0.05. All statistical analyses were performed using the SPSS software, version 29.0 (IBM Statistics, Greece).

3. Results

All neonates completed the trial and were incorporated in the final analyses, without any dropouts. The study sample comprised 100 newborns meeting the SGA criteria (see Fig. 1). The control group, consisting of 50 neonates, adhered to the regimen established by the protocols with weight calculations based on the actual birth weight, while the intervention group of 50 neonates followed the identical regimen, with weight calculations based on the 10th percentile.

In Table 1, the characteristics of the N = 100 SGA neonates are depicted. No differences were observed between the two groups regarding gestational age, sex, birth weight, length at baseline and level of prematurity (all p's > 0.05).

In Table 2, the characteristics of the PN solution at baseline and at the endpoint (last day of PN) among the two neonate groups are presented. As expected, at baseline, the composition of the PN solutions differed between the two groups, as nutrient calculations were different (actual vs. corrected body weight) among the two groups. Accordingly, on both the first and the last day of PN, the macronutrient composition of the solutions differed significantly between the two groups. More specifically, in the intervention group, the daily administered amounts of energy, fluids, glucose, amino acids and lipids were higher than those administered to the control group at both time points (all p's < 0.05). On the other hand, daily administration of calcium, potassium, magnesium, sodium, and phosphorus concentrations were higher in controls than the intervention group at both points (all p's < 0.05). No statistically significant differences were observed in trace elements or in fat-soluble and water-soluble vitamins between the two groups (all p's > 0.05).

When comparing the composition of PN between the first and last day within each group (Table 2), the control group showed a decrease in daily amounts of amino acids, a marginally statistically significant increase in lipids, and significant increases in trace elements, fat-soluble and water-soluble vitamins, as well as phosphorus (all p's < 0.05). No other significant differences were found in the control group. The same pattern was observed in the intervention group, except for sodium, for which a statistically significant difference was detected (p = 0.024).

As depicted in Table 3, no statistical differences were found in the number of hospitalization days and the duration of PN between the control and the intervention group (all p's > 0.05).

In Table 4, anthropometrical characteristics of the 100 SGA neonates at both baseline and endpoint (last day of PN) are presented. At the beginning of the PN, the median weight of the newborns in the control and the intervention group had no statistically significant difference (p = 0.229). The same was observed at the endpoint (median = 1.60 kg, IQR: 0.4 vs. 1.56 kg, IQR: 0.62 for the control and the intervention group, respectively). However, the median weight gain was greater in the intervention group [median weight gain = 0.16 kg] than that of the control group [median weight gain = 0.09 kg], p = 0.034. Similarly, the relative change in

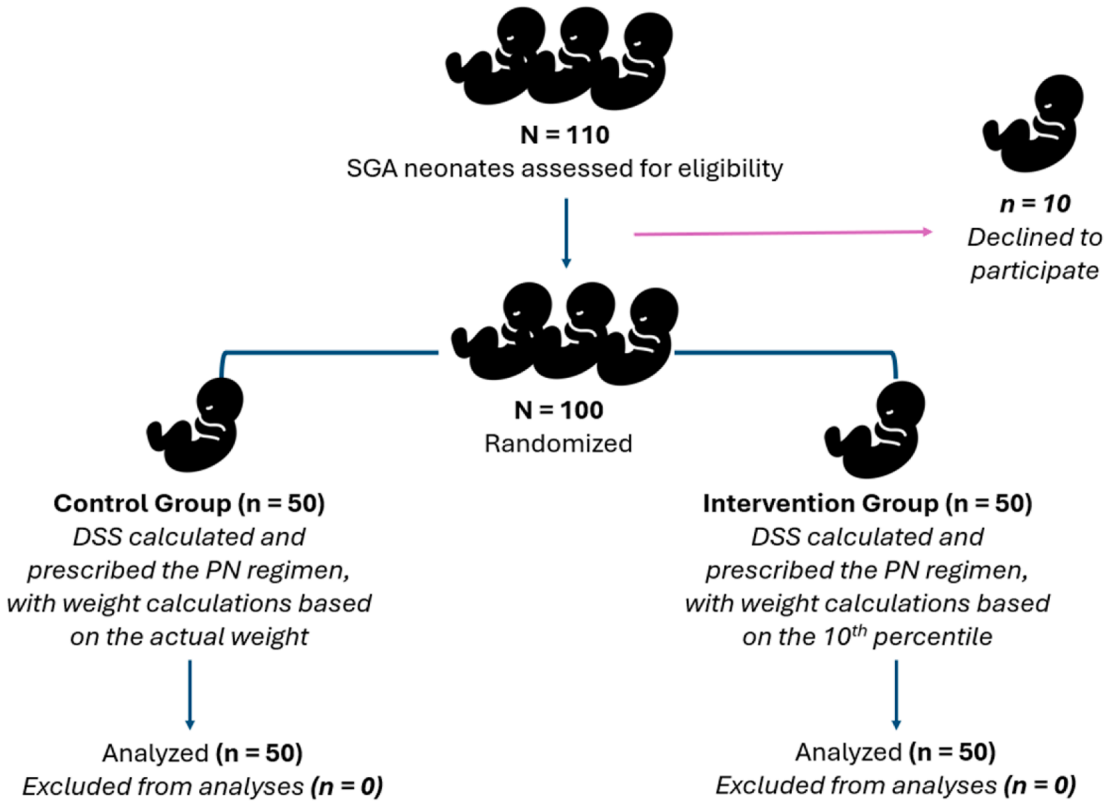

Fig. 1. CONSORT flow diagram and schematic overview of the design of the study.

body weight (% BW) was significantly higher in the intervention group (+13.6 %) than in the control group (+6.4 %), p = 0.047. In terms of length, both groups showed a significant increase during the PN (p = 0.001 and p = 0.002, respectively), with no statistically significant differences between them at the beginning (p = 0.350) or at the end of the intervention (p = 0.134). Similarly, for head circumference, both groups showed a significant increase (all p's < 0.05), but no difference was recorded between the groups (all p's > 0.05).

With regard to blood analysis (**Supplementary Table**), no differences in electrolytes, albumin and haematologic indices were observed between the two groups at the last day of PN (all p's > 0.05).

4. Discussion

This randomized controlled trial aimed to determine the optimal approach for estimating nutritional needs. More specifically, with the assistance of CDSS, nutrient estimations based on the neonates' actual weight were compared to those calculated using the weight corresponding to the 10th percentile of the growth curve, in order to identify which approach has the most favorable growth outcomes. The results showed that, although both groups showed normal increases in weight, length, and head circumference, the intervention group showed significantly greater weight gain at the end of the PN.

It was revealed that the two groups of SGA neonates did not differ significantly in terms of sex, gestational age, birth weight, and body length. This may suggest that the groups were initially homogeneous and therefore the differences observed in the results were likely attributed to the different nutritional estimation approaches through CDSS. It is well-documented that optimal nutrient provision plays a crucial role in the growth and development of SGA neonates, particularly in the NICU setting [24,25]. Numerous studies support that precise nutrient delivery, aligned with the unique metabolic needs of SGA infants, can prevent

Table 1
Characteristics of the 100 SGA neonates enrolled in the study at baseline.

Characteristics	Overall (N = 100)	Control Group (n = 50)	Intervention Group (n = 50)	p-value
Sex (females) *n (%)*	51 (51)	23 (46)	28 (56)	0.317
Gestational age (weeks) *Median (IQR)*	33 (4.0)	34 (3.0)	33 (4.0)	0.159
Prematurity *n (%)*				
Moderate to late preterm (32–37 weeks)	71 (71)	39 (78)	32 (64)	0.169
Very preterm (28–32 weeks)	24 (24)	8 (16)	16 (32)	
Extremely preterm (<28 weeks)	5 (5.0)	3 (6.0)	2 (4.0)	
Length (cm) *mean (SD)*	38 (2.7)	39 (3.2)	38 (1.9)	0.383
Birth weight (kg) *Median (IQR)*	1.41 (0.6)	1.44 (0.59)	1.30 (0.6)	0.222

Categorical values are presented as frequencies (%) and continuous as mean and standard deviation (SD) if normally distributed or median and interquartile range for skewed variables. p-values derived from Student's t-test or Mann–Whitney U test for normally distributed and skewed continuous variables, respectively, or the chi-square test for the categorical variables. Statistical significance was set at p-value <0.05.

Table 2
Characteristics of the PN solution at baseline (1st day of PN) and at the endpoint (Last day of PN) among the control (n = 50) and the intervention (n = 50) groups.

Characteristics	Time	Control Group (n = 50) Median (IQR)	Intervention Group (n = 50) Median (IQR)	p^1
PN energy (kcal/day)	1st day of PN	62 (42)	105 (47)	**<0.001**
	Last day of PN	52 (62)	108 (89)	**0.014**
p^2		*0.932*	*0.784*	
PN fluids (ml/day)	1st day of PN	107 (39)	152 (48)	**<0.001**
	Last day of PN	78 (85)	171 (112)	**0.01**
p^2		*0.258*	*0.607*	
PN glucose (g/day)	1st day of PN	12 (7.0)	16.5 (4.2)	**<0.001**
	Last day of PN	8.7 (9.9)	17.9 (12)	**0.019**
p^2		*0.144*	*0.819*	
PN amino acids (g/day)	1st day of PN	2.8 (1.9)	4.48 (1.22)	**<0.001**
	Last day of PN	1.8 (2.1)	3.7 (3.3)	**0.012**
p^2		***0.038***	***0.009***	
PN lipids (g/day)	1st day of PN	0.90 (3.0)	3.7 (4.1)	**0.003**
	Last day of PN	1.8 (2.1)	3.7 (3.3)	**0.007**
p^2		*0.05*	*0.661*	
Calcium (mEq/day)	1st day of PN	2.53 (0.8)	1.5 (0.99)	**<0.001**
	Last day of PN	3.0 (1.98)	1.4 (1.25)	**0.006**
p^2		*0.378*	*0.914*	
Trace elements (ml/day)	1st day of PN	0.0 (0.0)	0.0 (0.0)	0.337
	Last day of PN	0.0 (0.56)	0.47 (0.41)	0.087
p^2		***0.003***	***<0.001***	
Potassium (meq/day)	1st day of PN	3.3 (3.2)	0.0 (2.4)	**<0.001**
	Last day of PN	2.3 (2.2)	1.2 (1.0)	**0.005**
p^2		*0.263*	*0.286*	
Fat-soluble vitamins (ml/day)	1st day of PN	0.0 (0.0)	0.0 (0.0)	0.337
	Last day of PN	4.0 (3.4)	2.8 (3.0)	0.200
p^2		***<0.001***	***<0.001***	
Magnesium (mEq/day)	1st day of PN	0.9 (0.9)	0.39 (0.74)	**0.002**
	Last day of PN	1.0 (0.8)	0.48 (0.42)	**0.005**
p^2		*0.134*	*0.082*	
Sodium (mEq/day)	1st day of PN	3.1 (2.8)	1.41 (2.32)	**<0.001**
	Last day of PN	4.0 (2.6)	1.85 (1.74)	**0.017**
p^2		*0.065*	***0.024***	
Water-soluble vitamins (ml/day)	1st day of PN	0.0 (0.0)	0.0 (0.0)	0.337
	Last day of PN	1.76 (1.48)	1.23 (1.31)	0.200
p^2		***<0.001***	***<0.001***	
Phosphorus (mmol/day)	1st day of PN	1.38 (1.4)	0.6 (1.15)	**0.004**
	Last day of PN	1.9 (1.2)	0.87 (0.76)	**0.014**
p^2		***0.02***	***0.012***	

Results are presented as median and interquartile ranges. p^1: p-value for group comparison (Mann–Whitney U test), p^2: p-value for time effect (Wilcoxon signed-rank test). bold p's indicate statistically significant differences. Statistical significance was set at p-value <0.05.

Table 3
Number of hospitalization days and duration of PN of the 100 SGA neonates.

Characteristics	Overall (N = 100)	Control (n = 50)	Intervention (n = 50)	p-value
Days of hospitalization (days) *mean (SD)*	31 (23)	29 (18)	34 (28)	0.413
PN duration (days) *mean (SD)*	12 (8)	12 (10)	16 (10)	0.082

Values are presented as mean and standard deviation (SD) if normally distributed or median and interquartile range for skewed variables. p-values derived from Student's t-test or Mann–Whitney U test for normally distributed and skewed continuous variables, respectively. Statistical significance was set at p-value <0.05.

growth deficiencies and reduce risks of long-term developmental impairments [26]. Mechanistically, adequate nutrient intake supports cell proliferation, organ maturation, and metabolic stability in SGA infants, whose nutrient stores and metabolic reserves are often compromised due to intrauterine growth restrictions. Precise nutrient delivery ensures a balanced supply of proteins, carbohydrates, lipids, vitamins, and minerals necessary for tissue growth and neural development [27,28].

In the present study, since the nutritional estimations were based on the actual weight of the neonates and the weight corresponding to the 10th percentile (corrected weight), it was found that the composition of the PN solutions differed significantly between the two groups. In the intervention group (corrected weight), the amounts of energy, protein, carbohydrates, and lipids administered were systematically higher than in the control group. This may indicate that this CDSS, when using corrected weight, specifies increased requirements, which may more realistically reflect the growth needs of SGA infants. Significant differences in fluids and minerals were observed reflecting the osmolarity limitations and fluid balance in PN solutions as guided by ASPEN recommendations [21]. No difference was observed in trace elements or vitamins, suggesting that the system maintains a constant ratio of micronutrients regardless of reference weight. Actually, it has been already suggested that CDSS tools may minimize human errors and provide better real-time interventions for neonatal growth [15]. Besides, CDSS tools may enhance protein delivery in preterm infants [29] and overall neonatal care [30].

Additionally, the intervention group showed a greater increase in body weight and a greater relative weight change, meaning a faster daily weight growth. The observed difference in weight gain

Table 4
Anthropometrical characteristics of the 100 SGA neonates at baseline and at the endpoint.

Characteristics	Time	Control Group (n = 50)	Intervention Group (n = 50)	P^1
Body weight (kg)	1st day of PN	1.44 (0.57)	1.25 (0.59)	0.229
	Last day of PN	1.60 (0.43)	1.56 (0.59)	0.918
P **²**		**<0.001**	**<0.001**	
Weight difference (kg)		+0.09 (0.21)	+0.16 (0.30)	**0.034**
Relative change in BW (%)		+6.7 (21)	+13.8 (23)	**0.047**
Body length (cm)	1st day of PN	38.6 (3.2)	37.7 (1.9)	0.350
	Last day of PN	46.2 (1.59)	44.3 (3.4)	0.134
P **²**		**0.001**	**0.002**	
Length difference (cm)		7.6 (3.1)	6.6 (3.2)	0.273
Head circumference (cm)	1st day of PN	27.5 (2.1)	27.2 (1.3)	0.658
	Last day of PN	33.2 (1.1)	32.4 (1.4)	0.067
P **²**		**0.001**	**0.002**	
Head circumference difference (cm)		5.5 (2.2)	5.2 (2.1)	0.628

Continuous variables are presented as mean and standard deviation (SD) or median and interquartile range. p^1: p-value for group comparisons, derived from Student's t-test or Mann–Whitney U test. p^2: p-value for time effect, using paired samples t-test or the Wilcoxon test. bold p's indicate statistically significant differences. Statistical significance was set at p-value <0.05.

between the two groups could be considered clinically important, as even modest improvements in early postnatal weight gain in SGA neonates have been associated with improved neurocognitive and metabolic outcomes, as well as reduced risk of postnatal growth failure [31]. The magnitude of weight gain observed in the intervention group is in line with other studies suggesting the importance of optimized energy and protein provision in this high-risk population [32].

In contrast, length and head circumference did not differ significantly between the groups at the last day of PN, which is to be expected, as these changes take longer to become apparent. Actually, there is evidence suggesting that low weight newborns have slower weight and length gain and head circumference increase, compared to normal weight newborns [33]. In accordance with our study, Embleton et al. (2001) suggested that providing nutrients based on RDIs (recommended dietary intake) may lead to significant energy and protein deficits and could be associated with postnatal growth retardation in premature infants [34]. This finding supports the need for a more “aggressive” or tailored nutritional approach, especially in SGA infants for better growth-related outcomes. In the present study, no significant difference was observed regarding albumin blood levels, which may reflect that were documented. This is in accordance with Embleton et al. (2001), who showed that serum albumin did not correlate with nutritional intake or growth velocity in preterm infants [34].

To the best of our knowledge, this is one of the first randomized controlled trials exploring the effects of a CDSS tool on SGA neonate growth using two different nutritional estimation approaches (i.e., based on the actual weight or the weight corresponding to the 10th percentile of weight curve). However, the current trial has some limitations. The single-center design of the study may limit the generalizability of the findings to other NICU settings. The duration of follow-up was limited to the days of PN without monitoring the newborns during the enteral feeding phase or after the discharge from the NICU setting. This does not allow assessing the long-term effect of the intervention on children's growth. In general, it is highly recommended for SGA infants to be monitored since they are more prone to have obesity and metabolic syndrome in adulthood [35]. As biochemical monitoring followed routine clinical practice, additional metabolic markers (e.g. phosphorus and magnesium) that may provide further insight into nutritional adaptation in SGA neonates were not available for analysis. Therefore, the results of this randomized controlled trial should be interpreted with caution.

5. Conclusions

To conclude, macronutrient composition of PN solution based on the corrected weight to the 10th percentile estimation of weight for SGA neonates may result in adequate provision of energy and nutrients, as reflected by greater weight gain in the present study. Therefore, the use of a specialized CDSS may facilitate individualized PN prescriptions and support safer and more beneficial nutritional management in SGA neonates. Therefore, nutrient estimations based on the 10th percentile of weight applied by the CDSS tool, appear to be the most favorable combination for faster weight gain among SGA neonates.

Author contributions

Conceptualization, A.G.; methodology, P.P., A.G. and A.F.; validation, A.G., A.F., P.P.; formal analysis, E.B. and A.F.; investigation, P.P., E.B.; data curation, P.P., E.B., A.G.; writing—original draft preparation, A.F.; writing—review and editing, P.P., A.G., A.F.; supervision, A.G.; All authors have read and agreed to the published version of the manuscript.

Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to their containing information that could compromise the privacy of the research participants.

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Conflict of interest

Panos Papandreou PharmD PhD, created the CDSS called Nutrinet Parenteral.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2026.102960.

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