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Trabajo Original

Pediatría

Weight gain speed and z-score behavior in large prematures for gestational age

Velocidad de aumento de peso y comportamiento de la puntuación z en prematuros grandes para la edad gestacional

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Abstract

Objective: to investigate the speed of weight gain (WG) and the z-score (E-z) of weight in premature neonates large for gestational age (LGA) during four weeks of hospitalization.

Methods: a retrospective longitudinal study with premature neonates in a neonatal intensive care unit at a university hospital. Data were obtained from January 2017 to December 2018; 115 babies with gestational age (GA) ≥ 27 and < 37 weeks, non-twin, AGA or LGA were included. The WG (g/kg/day) was obtained from the nadir weight and the E-z was calculated online based on the Intergrowth-21st curves. Repeated-measures ANOVA and multiple linear regression were used to assess the association between WP and E-z and explanatory variables; p < 5 %.

Results: mean GA was 32.5 weeks, birth weight was 1910 g and weight loss was 5 % at 7 days. WG was lower in LGA babies, with GI between 32 and 37 weeks (LGA, 9.2 ± 5.6 g/kg/day vs AGA, 13.9 ± 6.0 g/kg/day). The change in WG was explained by protein supply in AGA (B = 2.5 g/kg/day; 95 % CI, 0.7 to 4.3; and β = 0.543) and by GA in LGA (B = -0.05 g/kg/day; 95 % CI, -0.09 to -0.02; and β = -0.574). In the 4th week of hospitalization, weight E-z decreased similarly for LGAs and AGAs, and this variation was explained by growth.

Conclusions: premature LGAs had lower WG compared to AGAs during the neonatal period. The linear and brain growth explained the variation in weight E-z among these preterms.

Keywords:

Premature newborn. Nutritional status. Weight gain. Nutritional assessment.

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Resumen

Objetivo: investigar la velocidad de la ganancia de peso (GP) y la puntuación z (E-z) de peso en neonatos prematuros grandes para la edad gestacional (GEG) durante cuatro semanas de hospitalización.

Métodos: estudio longitudinal retrospectivo con neonatos prematuros de una unidad de cuidados intensivos neonatales de un hospital universitario. Los datos se obtuvieron desde enero de 2017 hasta diciembre de 2018. Se incluyeron 115 bebés con edad gestacional (EG) ≥ 27 y < 37 semanas, no gemelos, AEG o GEG. El GP (g/kg/día) se obtuvo a partir del peso nadir y el E-z se calculó en línea basado en las curvas Intergrowth-21st. Se utilizaron el ANOVA de medidas repetidas y la regresión lineal múltiple para evaluar la asociación entre GP y E-z y las variables explicativas; p < 5 %.

Resultados: la EG media fue de 32,5 semanas, el peso al nacer de 1910 g y la pérdida de peso del 5 % a los 7 días. El GP fue menor en los bebés GEG, con EG entre 32 y 37 semanas (GEG: 9,2 ± 5,6 g/kg/día *vs.* AEG: 13,9 ± 6,0 g/kg/día). El cambio en el GP se explicó por el suministro de proteínas en los AEG (B = 2,5 g/kg/día; IC 95 %: 0,7 a 4,3; y β = 0,543) y por EG en los GEG (B = -0,05 g/kg/día; IC 95 %: -0,09 a -0,02; y β = -0,574). En la 4ª semana de hospitalización, el peso E-z se redujo de manera similar en los GEG y los AEG, y esta variación se explicó por el crecimiento.

Conclusiones: los prematuros GEG tuvieron un menor GP en comparación con los AEG durante el periodo neonatal. El crecimiento lineal y cerebral explicó la variación del peso E-z de estos prematuros.

Palabras clave:

Recién nacido prematuro. Estado nutricional. Aumento de peso. Evaluación nutricional.

INTRODUCTION

Prematurity accounts for 35% of neonatal deaths and important complications that compromise the life trajectory of those born prematurely (1). In Brazil, 12% of births are premature and this is a relevant factor for the global burden of chronic diseases in the population (2,3).

The extremes of nutritional status at birth, small (SGA) or large for gestational age (LGA), are associated with an even higher risk of neonatal death and disease later in the preterm infant's life (1-4). The overall prevalence of LGA preterm infants is estimated to be 6%, but this rate triples when the mothers are diabetic (3,5,6).

LGA preterm infants in particular are attributed a higher chance of increased adiposity and risk of developing cardiometabolic and neurological diseases when compared to gestational age-appropriate (AGA) preterm infants (1,4-6). However, the number of studies on the growth of preterm LGA infants in the neonatal period, as well as its long-term consequences, is limited (1,4).

The reference for adequate growth of preterm infants is the intrauterine rate, but the effort to maintain this rate in the extrauterine environment is an arbitrary conduct, particularly for LGA preterm infants (4). In these infants epigenetic mechanisms associated with the rapid supply of nutrients would be the principal determinants of the increased number and size of fat cells in the extrauterine environment (1,4,6,7).

Current studies indicate that the accelerated rate of weight gain in preterm LGA infants triggers, already in the neonatal phase, a change in body composition, with consequent increase in fat mass, and metabolism alterations in these infants. Therefore, nutrition offered especially in the first four weeks of life is an important factor mediating the speed of weight gain in these preterm (1,4,7).

The objective of this study was to investigate the rate of weight gain and the z-score of weight in preterm neonates large for gestational age, during four weeks of hospitalization in a university hospital in southern Brazil.

METHODS

Retrospective longitudinal study, carried out with premature neonates admitted to the neonatal intensive care unit (NICU) of a university hospital in southern Brazil. Data from premature neonates born during the period January 2017 to December 2018 was analyzed. We included premature neonates with gestational age (GA) ≥ 27 and < 37 weeks, of both sexes, non-twin, classified according to birth weight as AGA or LGA, hospitalized for ≥ 1 week, who did not have conditions altering growth and anthropometry such as micro and hydrocephalus, chromosomopathies, fetal hydrops and congenital malformations. Of the 115 eligible premature neonates, 54, 36, and 27 remained in the study during the second, third, and fourth week of hospitalization, respectively. Discharge from the unit was the main reason for loss to follow-up, and there were two deaths during the second week of hospitalization (Fig. 1).

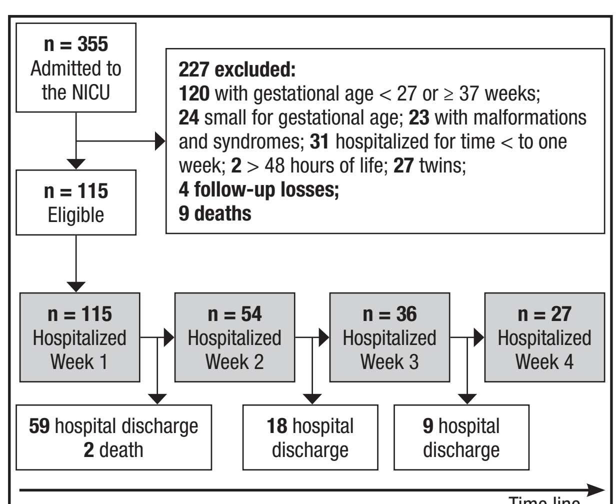

Figure 1.

Recruitment and follow-up of the study preterms.

Demographic, clinical, nutritional and anthropometric variables were obtained from the NICU records by nutritionists of the service. The GA was estimated in order of priority by i) maternal information on the date of the last menstrual period (Naegele's Rule, which considers the normal gestation time of 280 days), when it differs by a maximum of two weeks from the GA provided by fetal ultrasonography performed up to 20 weeks of gestation; ii) ultrasonography performed up to 20 weeks of gestation, in cases where the maternal GA was not considered reliable and the difference between the ages calculated by ultrasonographic methods and the New Ballard was less than two weeks or iii) postnatal GA calculated by the New Ballard Method, when it differed by more than two weeks from the maternal and ultrasonographic GA (8,9).

The main outcome studied was the rate of weight gain (g/kg/day) calculated with the equation: [(*current weight* - *previous weight*)/([(*previous weight* + *current weight*)/2]/1000)/number of days], being the weight in grams, from the lowest weight during the neonatal period. Velocity was calculated until the fourth week of hospitalization (10). Anthropometric measurements were performed by previously trained NICU staff following the recommendations described by the World Health Organization (WHO) in the Anthropometry Handbook (11). The weight (P) in grams was measured on a Filizola Baby® electronic scale (whit approximation of 5g), after weighing, discounting any equipment attached to the newborn. The length (L) in centimeters was obtained on a SECA 210 portable anthropometer (with 5mm graduation), with the newborn in dorsal decubitus position, in Frankfort's horizontal plane, with one end fixed (cephalic) and the other mobile (podalic), with the help of another person holding the newborn. Cephalic circumference (CP) in centimeters was measured with an inextensible measuring tape (whit approximation 0.1 cm), taking into account the largest occipitofrontal diameter. Nutritional status at birth was obtained based on the reference curves for GA according to INTERGROWTH-21st. Preterm infants whose birth weight was between the 10th and 90th percentiles of the curve were considered AGA, and those with birth weight above the 90th percentile were considered LGA (12).

The secondary outcome was the z-score (E-z) of weight according to sex and GA. The E-z value was obtained using the Intergrowth-21st manual online calculator for preterm infant body dimensions, available at: http://intergrowth21.ndog.ox.ac.uk/preterm/en/ManualEntry).

The exposure variables were GA collected in weeks and days and categorized into ≥ 27 to < 32 and ≥32 to < 37 weeks, birth weight (grams) categorized into <1,500 g and ≥ 1. 500 g, sex (female and male), APGAR value attributed from 1 to 10 points, the percentage of weight loss obtained by the equation: {[(current-previous weight)/previous weight]x100}, the E-z of length and cephalic perimeter, daily energy intake (kcal/kg) and protein (g/kg) calculated considering the total nutrient supply, provided by parenteral nutrition (PN) and enteral nutrition (EN). To calculate the caloric and protein intake provided by parenteral nutrition, infant formulas (IF) and additives, the information contained on the product label was used; for breast milk, the calculations were performed considering the chemical composition values of premature breast milk, according to the week after birth, as informed by the Ministry of Health (13). The volume considered was the volume actually administered in 24 hours.

Data were double keyed in the EpiData® version 3.1 for later analysis of consistency of the data entry and the analyses were conducted in the statistical package Stata® version 12. Descriptive analyses are presented as mean ± standard deviation for continuous variables and proportions for categorical variables. Since the outcome variables had a symmetrical distribution, the comparison between categories was performed using parametric tests. The comparison between the categories of nutritional status AGA and LGA over the duration of hospitalization was performed using the test of variance, repeated measures ANOVA, followed by Bonferroni *post hoc.* For that, the assumptions of homoscedasticity, independence and sphericity of the residuals were analyzed. Linear regression was used to evaluate the association between speed of weight gain and explanatory variables. In this case the variables tested were: GA at birth, birth weight, energy intake, and protein intake. Only variables associated with a statistically significant change in β value were kept in the regression model. Linear regression was also used to investigate the association between the E-z for weight and the E-z for height and head circumference at weeks 2, 3 and 4. We kept in the regression model only those variables that showed a statistically significant change in the β value. The statistical significance level adopted was $p < 5\%$.

The study was approved by the Ethics and Research Committee of the Medical School, under number 1.639.674, through Plataforma Brazil.

RESULTS

Of the 115 premature neonates included in the study 44 % were classified as LGA and 54% were male. Most had neonatal respiratory distress syndrome (73%) and 25% had neonatal sepsis. In the first week of hospitalization 78% were receiving milked breast milk + infant formula and at the end of the study 63% were receiving this type of feeding. There was no statistically significant association between nutritional status at birth and the supply of milked breast milk during the study (data not shown in tables and figures).

The mean GA at birth, APGAR, weight, length and head circumference were 32.5 weeks, 8.0, 1910 g, 41.7 cm and 29.8 cm, respectively. At 7 days of hospitalization the mean weight loss was 5%. The mean GA was statistically lower in LGA preterm neonates (31.8 ± 2.9 weeks), compared to AGA (33.1 ± 2.1 weeks). As for E-z, in AGA preterm infants there was a reduction of 0.886 E-z for weight and 1.045 E-z for CP between admission and the first week of hospitalization. In this period, the reduction was 0.973 E-z for weight and 0.918 E-z for CP among LGA. The energy intake received by both preterm infants increased significantly at weeks 1 and 4 (AGA week 1, 2, 3 and 4, respectively 67.3 ± 25.3, 93.3 ± 23.2, 92.6 ± 28.1, 103.0 ± 41.1;

LGA week 1, 2, 3 and 4, respectively 70.1 ± 25.7, 102.0 ±14.9, 99.3 ± 30.3 and 113.9 ± 24.2) compared to admission (AGA 7.0 ± 11.4 and LGA 11.2 ± 9.4 (Table I).

Mean weight gain was statistically significantly greater in preterm neonates born at 27 to 31 weeks (AGA 16.6 ± 2.9 g/kg/day; LGA 15.1 ± 5.6 g/kg/day) compared to those born at 32 to 37 weeks (AGA 13.9 ± 6.0 g/kg/day; LGA 9.2 ± 5.6 g/kg/day). However, at 32 to 37 weeks, the mean weight gain was statistically significantly lower in LGA infants (9.2 ± 5.6 g/kg/day) compared to AGA infants (13.9± 6.0 g/kg/day) (Table II).

The correlation coefficient between relative weight gain and GA at birth was negative, moderate and statistically significant for LGA preterm neonates, r = -0.521 (data not shown in tables and figures).

Table III shows the regression coefficients of the speed of weight gain. In preterm AGA neonates, protein supply was the variable that significantly explained the change in speed of weight gain (B 2.5 g/kg/day, 95% CI 0.7; 4.3 and β 0.543). In the LGA, the GA was the variable that significantly explained the change in the speed of weight gain (B -0.05 g/kg/day, 95% CI -0.09; -0.02 and β -0.574).

The dynamics of the speed of weight gain and weight E-z are shown in figure 2. For both groups, at the fourth week of hospitalization, a lower mean E-z weight was observed (AGA -1.58; LGA -0.280 E-z) compared to that at the second and third week of hospitalization (AGA -1.18 and -1.30 E-z, respectively; LGA, 0.20 and 0.032 E-z, respectively) (Fig. 2A). As for the rate of weight gain, for both groups of preterm infants, after the weight

Table I. Characteristics of premature infants according to nutritional status at birth. Neonatal Intensive Care Unit. HE-UFPEL/EBSERH, Pelotas, 2017-2018 (n = 115)

	All			AGA			LGA			p
	n	Mean	sd	n	Mean	sd	n	Mean	sd	
Gestational age (weeks)	115	32.5	2.6	64	33.1	2.1	51	31.8	2.9	0.008‡
APGAR[a]	111	8.0	1.0	63	8.0	1.1	48	8.0	1.0	0.488‡
Birth weight (g)	115	1910.9	605.5	64	1847.1	493.4	51	1990.9	719.3	0.207‡
Length at birth (cm)	115	41.7	3.9	64	41.6	3.6	51	41.8	4.4	0.889‡
Cephalic perimeter at birth (cm)	115	29.8	3.1	64	29.8	2.9	51	29.8	3.4	0.887‡
Weight loss (%)[b]	113	5.0	5.1	63	4.2	4.9	50	5.7	5.2	0.120‡
Z-score										
Weight										
Admission	115	0.8	0.9	64	0.1	0.6	51	1.5	0.5	< 0.001[α]
Week 1	113	-0.2	0.9	63	-0.8	0.6	50	0.6	0.7	< 0.001[β]
										< 0.358[ω]
Length										
Admission	115	0.2	1.1	64	-0.3	0.9	51	0.8	0.9	0.556[α]
Week 1	91	0.3	1.2	46	-0.4	0.9	45	0.9	1.0	< 0.328[β]
										< 0.579[ω]
Cephalic perimeter										
Admission	115	0.2	1.2	64	-0.2	1.0	51	0.7	1.2	< 0.001[α]
Week 1	92	-0.9	1.3	47	-1.4	1.1	45	-0.3	1.3	< 0.001[β]
										< 0.578[ω]
Nutritional care										
Start of minimum enteral nutrition (h)	93	15.5	25.1	57	16.8	29.4	36	13.4	16.4	0.522†
Energy (kcal/kg/day)										
Admission	91	8.6	15.1	55	7.0	11.4	36	11.2	9.4	< 0.001[α]
Week 1	103	68.6	25.4	56	67.3	25.3	47	70.1	25.7	< 0.091[β]
Week 2	46	97.6	19.8	23	93.3	23.2	23	102.0	14.9	< 0.678[ω]
Week 3	29	95.6	28.7	16	92.6	28.1	13	99.3	30.3	
Week 4	24	109.8	31.2	9	103.0	41.1	15	113.9	24.2	

n: number of preterm infants; AGA: birth weight classified as adequate for gestational age; LGA: birth weight classified as large for gestational age. [a]APGAR index; [b]% weight loss at 7 days of hospitalization; †Student's t-test; [α]Comparison between lengths of hospitalization, ANOVA of repeated measures; [β]Comparison between AGA and LGA, ANOVA of repeated measures; [ω]Interaction between time of hospitalization and birth size, ANOVA of repeated measures.

Table II. Rate of weight gain according to nutritional status and according to gestational age, birth weight and sex of preterm infants. Neonatal Intensive Care Unit. HE-UFPEL/EBSERH, Pelotas, 2017-2018 (n = 49)

	n	%	ALL		AGA		LGA		p
			g/kg/day		g/kg/day		g/kg/day		
			Mean	Sd	Mean	Sd	Mean	Sd	
Gestational age (weeks)									
27 a 31	25	51	15.7	4.8	16.6	2.9	15.1	5.6	0.010$^{\alpha}$
32 a 37	24	49	12.3	6.1	13.9	6.0	9.2†	5.6	0.049$^{\beta}$
Birth (g)									
< 1500 g	26	53	15.8	4.4	17.8	3.8	14.4	4.5	0.974$^{\alpha}$
≥ 1500 g	23	47	12.0	6.4	17.4	5.0	14.6	10.5	0.506$^{\beta}$
Sex									
Female	24	49	13.0	5.4	14.5	5.0	11.0	5.6	0.176$^{\alpha}$
Male	25	51	15.0	5.9	15.3	5.6	14.7	6.3	0.240$^{\beta}$

n: number of preterms; AGA: adequate for gestational age; LGA: large for gestational age. $^{\alpha}$Comparison between gestational age categories or birth weight or sex, ANOVA; $^{\beta}$Comparison between AGA and LGA, ANOVA; †p = 0.013 between gestational age categories in the LGA group, Bonferroni.

Table III. Linear regression of the speed of weight gain according to the nutritional status of preterm infants. Neonatal Intensive Care Unit. HE-UFPEL/EBSERH, Pelotas, 2017-2018 (n = 49)

	Weight gain (g/kg/day)					
	B	β	B (95 % CI)		Adjusted R2	p
AGA						
Constant	7.4	ref				0.007
Protein (g/kg/day)	2.5	0.543	0.7	4.3[a]	26 %	
LGA						
Constant	22.5	ref				0.007
Gestational age (weeks)	-0.05	-0.574	-0.09	-0.02[b]	29 %	

AGA: adequate for gestational age; LGA: large for gestational age; β: regression coefficient. [a]Adjusted for protein (g/kg/day); [b]Adjusted for gestational age.

loss phase, the mean was statistically significantly higher in the third week of hospitalization (AGA 20.0 g/kg/day; LGA 19.9 g/kg/day) compared to the second week (AGA 11.7 g/kg/day; LGA 15.9 g/kg/day) (Fig. 2B).

Table IV shows the regression coefficients of E-z weight. It can be seen that in both groups the change in weight E-z was statistically explained by linear and encephalic growth during hospitalization. In LGA preterms, the change in weight E-z observed at week 2 (B 0.381, 95 % CI 0.192;0.570 and β 0.737), 3 (B 0.357, 95 % CI 0.029; 0.684 and β 0.633) and 4 (B 0.461, 95 % CI 0.070; 0.853 and β 0.691) was explained by length E-z. In AGA preterm neonates the head circumference E-z significantly explained the change in weight E-z at the second (B 0.243, 95 % CI 0.057;0.428 and β 0.508) and third (B 0.267, 95 % CI 0.046;0.487 and β 0.420) week of admissiontion.

DISCUSSION

This study showed that preterm LGA neonates, especially those with higher GA, were characterized by a lower rate of weight gain than preterm AGA neonates in the first weeks of postnatal life. The GA and protein intake significantly explained the variation in the rate of weight gain in preterm LGA and AGA neonates, respectively. The difference in the E-z of weight was similar between LGA and AGA, and the change in this parameter was significantly explained by the increase in the E-z of height and head circumference, indicating growth of the infants (Fig. 3).

The study of growth dynamics in premature neonates is essential considering that extremes in postnatal growth velocity have been associated with deleterious outcomes on neurological, cardiovascular, and metabolic development (1,14). The reference

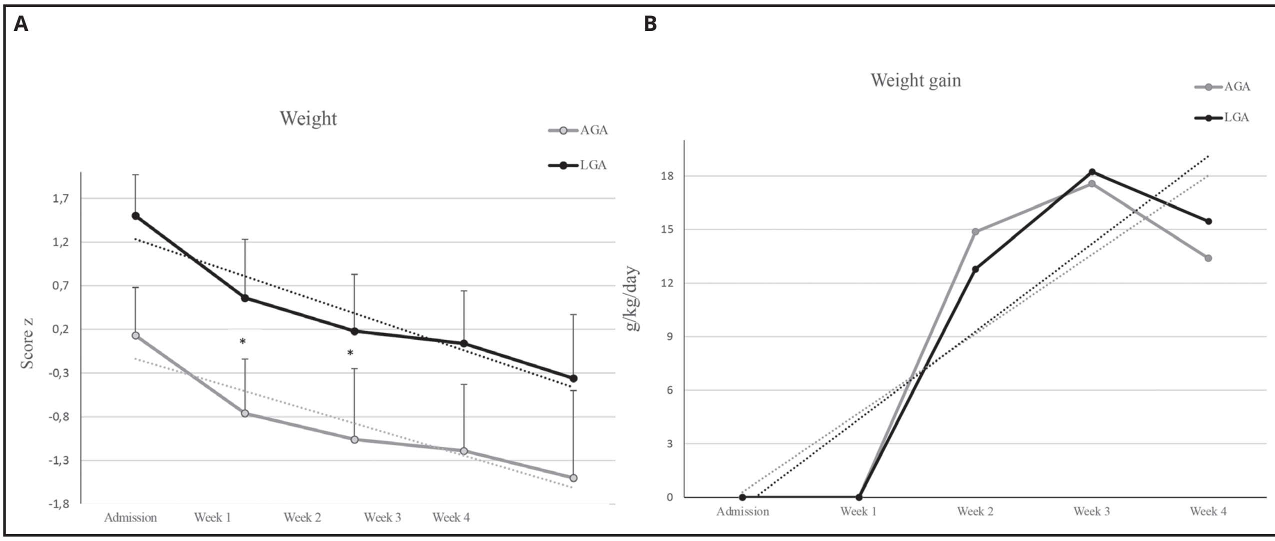

Figure 2.

Growth dynamics according to the nutritional status of premature infants. Neonatal Intensive Care Unit. HE-UFPEL/EBSERH, Pelotas, 2017-2018, N = 115, 49, 34 and 23, weeks 1, 2, 3 and 4, respectively. (A) Behavior of the weight z-score. (B) Speed of weight gain (g/kg/day) after weight loss phase. *$p < 0.05$ between LGA and AGA; **$p < 0.05$ between weeks 2 and 3 in the LGA group; repeated-measures ANOVA.

Table IV. Linear regression of the z-score of weight according to the nutritional status of prematures. Neonatal Intensive Care Unit. HE-UFPEL/EBSERH, Pelotas, 2017-2018 (n = 49)

	Weigth (Z-score)					
	B	β	B (95 % CI)		Adjusted R^2	p
AGA						
Week 2						
C E-z	0.461	0.508	0.170	0.752		0.004
PC E-z	0.243	0.420	0.057	0.428	54 %	0.013
Week 3						
PC E-z	0.267	0.541	0.046	0.487	58 %	0.021
LGA						
Week 2						
C E-z	0.381	0.737	0.192	0.570	51 %	0.000
Week 3						
C E-z	0.357	0.633	0.029	0.684	34 %	0.036
Week 4						
C E-z	0.461	0.691	0.070	0.853	36 %	0.026

AGA: adequate for gestational age; LGA: large for gestational age; β: regression coefficient.

for ideal postnatal weight gain for preterm infants has historically been the intrauterine rate, 15 g-20 g/ kg/day. Although widely employed, this recommendation has been questioned as to its applicability, biological plausibility, and the level of scientific evidence supporting it (1,4,7,14,15).

In the extrauterine environment the fetal growth rate is rarely achieved in the first weeks of life by premature infants because of the abrupt interruption of nutrients, time to reach full nutrition and physiological weight loss (4,7,10). Recent studies suggest that rapid energy and nutrient intake aimed at achieving "fetal growth" results in a higher transient proportion of body fat and increased adiposity in childhood (4,7).

Nutritional care of preterm infants is a challenge in clinical practice, and we must be aware of weight behavior as a variable

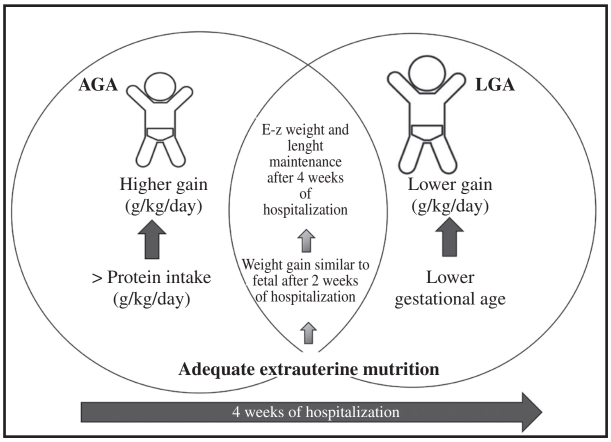

Figure 3.

Summary of the main results of the study.

part of a context, especially for those admitted to NICU. The best rate of weight gain for these preterm infants should be evaluated based on their individual trajectory after the weight nadir. Nevertheless, weight gain according to fetal gain thresholds is still considered an indicator of nutritional adequacy and overall well being of clincally stable preterm infants (5-7,10,11,14,16).

Proteins represent the second largest component of the body and are intensely metabolized in premature infants due to the high demand for essential and semi-essential amino acids for protein synthesis. During the neonatal period protein deficits can build up rapidly in premature babies. The body's protein content can decrease by up to 1.5%/day, in contrast to the normal growing fetus, which has a positive protein balance of ~ 2%/day. Amino acid intake, 3g/kg/day, before 5 days of life can minimize proteolysis and protein deficit and improve growth in premature infants (17,18).

To regain catch-up growth and brain development many preterm infants need more nutritional intake, but the amount and speed of this intake should be managed based on the individual trajectory of each baby, avoiding overfeeding, especially for LGA infants (4,19,20). In general, the weight catch-up of premature babies can occur before hospital discharge, but its speed depends, among other factors, on the type of food offered. In infants fed breast milk the catch-up may be slower and extend to 6 years of age. However, a more rapid "catch-up" in weight has been observed still in the neonatal period in formula-fed infants (19,20).

LGA preterm infants need monitoring of the rate of weight gain since they are at greater risk for acceleration in the postnatal period and increased adiposity in the later stages of life (6). Intrauterine exposure to excessive nutrition and an adverse environment, such as maternal obesity and/or gestational diabetes, are the initial events implicated in epigenetic modifications. Specifically, hypermethylation of the FGFR2 (Fibroblast Growth Factor Receptor Receptor 2) gene locus determines during all life stages an increased capacity to store energy and/or to form new fat cells (6,21).

Calculating the rate of weight gain is yet another challenge in premature care. In clinical practice, the use of different calculation methods results in interpretation errors and makes comparison between studies difficult (10,15). In order to have an adequate evaluation of this rate it is essential to define the period for obtaining the initial weight, the calculation method, and that the time between measurements is considered (10,15,16).

In the present study, the method of the average between two points, from the weight nadir, was used to calculate the rate of weight gain. For most babies, the nadir occurred at 7 days of postnatal life. In general, the growth of the premature neonates studied was close to the fetal rate.

Most studies do not recommend a regression to the birth percentiles, the that it makes sense to exclude the postnatal weight loss phase for the calculation. Identifying the nadir of weight is valuable information in the context of assistance (7,10,15). The E-z weight represents a measure of the distance from the median, which in this study was similar between the groups and indicated linear and encephalic growth (4,7,10,15).

This study has some limitations, such as the absence of information in the medical records and of sociodemographic and clinical data of the mother. However, we highlight as strengths a sample of clinically stable preterm neonates, the calculation of the rate of weight gain from the weight nadir and based on the two-point average method.

It was concluded that large preterm neonates showed a lower rate of weight gain than AGA preterm infants during the neonatal period. The weight E-z was analyzed in relation to the weight nadir and its variation was explained by linear growth in LGA preterm.

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