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Growth velocity of preterm appropriate for gestational age newborns

Lêni M. Anchieta,[1] César C. Xavier,[2] Enrico A. Colosimo[3]

Abstract

Objective: To assess the growth velocity of preterm appropriate-for-gestational-age newborns through growth curves.

Method: A longitudinal and prospective study was carried out at two state-operated maternity hospitals in Belo Horizonte. Two hundred and sixty appropriate for gestational age preterm infants with birth weight < 2,500 g were evaluated weekly for body weight, head circumference and length. Growth velocity curves were constructed based on the derivative of the mathematical equation of the Count's model applied to somatic growth. Two analyses were made in the present study: absolute velocity, i.e., weight gain (g/day), and head circumference and length gains (cm/week); and relative velocity, i.e., weight gain (g/kg/day), and head circumference and length gains (cm/m/week).

Results: The curves of weight gain (g/day) were proportional to birth weight (the lowest and the highest birth weight neonates gained 15.9 and 30.1 g/day, respectively). The curves of weight gain (g/kg/day) were inversely proportional to birth weight with increasingly higher rates of weight gain between the first and fourth weeks (during the third week, the lowest and the highest weight newborns gained 18 and 11.5 g/kg/day, respectively). Later there was a drop, and by the 12th week the rates were similar for all groups (7.5 to 10.2 g/kg/day). The curves of relative velocity (cm/m/week) for head circumference and length were inversely proportional to birth weight; the lower weight preterm newborns had, the higher head circumference and length growing rates were, compared with those with more weight.

Conclusion: The relative velocity is the best parameter to describe the growth dynamics of preterm infants, especially of those with lower birth weight. Lower birth weight infants gained more weight, head circumference and length.

J Pediatr (Rio J). 2004;80(5):417-24: Premature, growth curve, growth velocity.

Introduction

Birth weight and gestational age are strong prognostic factors both for the survival and the quality of life of a newborn. While many health care strategies have been developed to overcome the limitations of prematurity, the growth and nutritional support of such children remains a challenge. Achieving adequate growth and nutritional support in preterm and low weight newborn babies is often difficult during hospitalization, not just because of the metabolic and gastrointestinal immaturity, but also because of the compromised immune function and also because of other complicating medical conditions.[1,2] The reference scale used for optimum postnatal growth for preterm newborn babies has historically been rates of intra-uterine weight, length and head circumference gain for fetuses of the same gestational age,[3] However, a more exacting reference standard should include both growth rates and body composition for preterm newborn babies in adverse conditions; as is the case with the extra-uterine environment. Nevertheless, such a reference was not identified and could prove difficult to develop based on current knowledge.[4]

How to optimize premature newborns' growth during the neonatal period, and set them on a trajectory that is closer to that expected of their growth, reducing the prevalence of failure to thrive, should be decided individually, case by

1. Ph.D., Hospital das Clínicas, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil.
2. Ph.D.; Associate professor, UFMG, Belo Horizonte, MG, Brazil.
3. Ph.D. Associate professor, Department of Statistics, Institute of Sciences, UFMG, Belo Horizonte, MG, Brazil.

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case, depending on gestational age, physiological development, clinical progress and specific nutritional intervention.[5] What is important is that growth rates be available at all times and can be accelerated or reduced according to this assessment. One should, however, be cautious, particularly in relation to weight, with the use of absolute growth rates (g/day), which may not be suitable, giving a false impression of weight gain, whereas relative rates (g/kg/day) demonstrate that growth is adequate.[4] This study, by means of longitudinal and prospective observation of preterm newborn babies, from birth up to the twelfth week of life, aims at examining absolute gain velocity curves for weight (g/day), head circumference and length (cm/week) and relative gain velocity curves for weight (g/kg/day), head circumference and length (cm/m/week), under current neonatal care conditions in two public maternity units in Belo Horizonte.

Population, material and methods

A longitudinal study that included preterm, appropriate-for-gestational-age newborns, not twins or multiples, with birth weights less than 2,500 g, born at the *Odete Valadares* maternity unit at the *Fundação Hospitalar do Estado de Minas Gerais* (MOV/FHEMIG) and the *Otto Cirne* maternity unit at the *Hospital das Clínicas* at the *Universidade Federal de Minas Gerais* (HC/UFMG), from January to December 1996 (260) and whose mothers or guardians consented to take part. At an earlier date, the weight gain of appropriate-for-gestational-age newborns was assessed,[6] resulting in a publication focused on the weight gain velocity of preterm appropriate-for-gestational-age newborns.[7] Later, an assessment was made of somatic growth and growth velocity (weight, head circumference and length) of adequate and small for age newborn babies.[8] Newborn babies with congenital infections and/or severe congenital malformations, severe neurological conditions, unfavorable clinical progress that made measurement nonviable or interfered with parenteral and/or enteral nutrition, drug and chemical substance use by the mother, enteral feeding started after the first week of life and death during the study period. This investigation was approved by the Ethics Committee at the *Universidade Federal de Minas Gerais*.

Gestational age was estimated based on the gestational age calculated from information on the date of last menstruation, accepted as correct, and confirmed by ultrasound, performed before 20 weeks' pregnancy. If the difference between the information given by the mother and ultrasound was greater than one week, the gestational age as estimated by ultrasound took precedence. In cases of maternal uncertainty and the absence of ultrasound, age estimated by the date of last menstruation was confirmed by the clinical-neurological method,[9] accepting a difference of up to 2 weeks. In the absence of other information, just the clinical-neurological examination was used.[9]

The adequacy of intrauterine growth was assessed using curves developed by Lubchenco et al.,[10] and those newborn babies between the 10th and 90th percentiles were considered adequate for gestational age and those below the 10th percentile, small for gestational age.

Measurements for weight, head circumference and length were taken at birth, on the third day, and, from the seventh day onwards, weekly until the 84th day of life (12 weeks). Maximum admissible tolerance for these measurements was a maximum of 3 hours after birth, ±1 day on the third and seventh days and ±2 days from the 14th to the 84th days. Clinical progress, fluid and calorie intake were also monitored at the same intervals. The newborn babies were grouped according to birth weight at 250 g intervals, with the lower limit being 750 g (inclusive) and the upper 2,500 g, exclusive.

Nutritional management followed the normal routine for nutritional care and had the objective of meeting calorific requirements of 120-130 kcal/kg/day and fluid intake of 180-200 ml/kg/day, at the end of week 2. Parenteral nutrition, when indicated, was initiated from the third day onwards and withdrawn when the enteral component attained approximately 80 kcal/kg/day. During outpatients follow-up, maternal breastfeeding was always the first choice and when necessary formula for full term newborns was used.

Anthropometric measurements

The researchers took the weight, head circumference and length measurements (with the exception of the measurements taken at birth), during the morning, one hour before the first feed while the baby was still in hospital, and during the afternoon, always at the same time, during follow-up.

Weight was obtained with electronic scales (Filizola Baby, 15 kg capacity, minimum load 125 g, 5 g divisions and tare – 9 kg), calibrated twice-yearly, or when necessary by the service personnel.

Head circumference was measured by adjusting a flexible, unexpandable, millimeter steel measure to the child's head, passing the supraorbital region in front and the opisthocranion behind**.**

The newborn babies were measured with an anthropometric rule.[11] With the neonate in decubitus dorsal, one examiner adjusted the head of the child to the cephalic extremity, in contact with the vertex to the fixed plate, while a second examiner extended the legs and firmly pressed the soles of the feet against the moveable extremity.

Statistical model

The software Epi Info, version 6.0 was used to calculate means, medians and standard deviations. The database containing weight, head circumference and length data was subjected to statistical study with the objective of obtaining mathematical models which could explain the behavior of the longitudinal growth data and also of obtaining velocity curves. Hauspie[12] performs an excellent review of some of the mathematical models that are proposed in literature to explain the behavior of growth curves. From that paper the following models were selected:

1a. Second order polynomial:

$y = b_0 + b_1 * time + b_2 * time$

1b. Third order polynomial:

$y = b_0 + b_1 * time + b_2 * time + b_3 * time^3$

2. Logistic: $y = p + \frac{alpha}{1 + exp\ (b_0 + b_1 * time)}$

3. Monomolecular (Jenss-Baykey):

$y = alpha + p* time - exp(b_0 + b_1 * time)$

4. Count: $y = alpha + p* time + b_0 * LN\ (time + 1)$

where:

y is the estimated weight or head circumference or length (at each point)

b_0, b_1 and b_2 are estimated coefficients

p is the number of model parameters

The regression models cited above were adjusted by the least squares method using statistical software (SPSS). Models 2 and 3 have nonlinear parameters and require special adjustment routines. Models 1a, 1b and 4, however, have linear parameters and routines for their adjustment are included in all statistical software and even spreadsheets such as Excel. Parameters were estimated considering all sampling values as well as by taking just the means for each recording time. All predicted curves closely followed the observed curves. However, only Count's curve demonstrated a decrease in the second reading time (3 days). A numerical criterion extensively used to discriminate nonlinear regression models is the adjusted coefficient of determination, expressed as follows:

$$R^2_A = 1 - \left[\frac{n - 1}{n - p} \right] (1 - R^2)$$

where:

n: sample size,

p: number of model parameters,

R^2: adjusted coefficient of determination by least squares.

Count's model also behaved the best, according to this criterion, for the three variables under study. Therefore, based on these results, Count's model was chosen.

Growth velocity was analyzed in two different ways: absolute velocity, i.e. the rate of gain in weight (g/day), head circumference and length (cm/week); and relative velocity, i.e. the rate of gain in weight (g/kg/day), head circumference and length (cm/m/week). Absolute velocity was obtained using the mathematical equation derivative of Count's model:

$$\text{Growth rate} = p + \frac{b_0}{time + 1}$$

Using estimated parameter values (weight, head circumference and length) for the Count model, velocity curves were obtained for the different birth weight categories. For the weight variable, rates are negative (weight loss) until the seventh day and then positive for the remainder of the follow-up period. For this reason curves are given from the first week of life onwards. Rates for head circumference and length are negative in some birth weight categories, primarily for those newborn babies with lowest weights, but positive in others. This being so, it was decided to present these velocity curves from the first week of life on too.

Relative velocity was obtained by dividing the mean weight gain (g/day) by the mean weight (g) at each monitoring point, from the point at which original birth weight was attained once more until the end of the study. The head circumference and length variables were dealt with using the same methodology, but results were presented by weeks.

Figures 2, 3 and 8, presented in the results, are reproduced from the Brazilian Journal of Medical and Biological Research (2003;36:761-70) with the prior authorization of its editors.

Results

Two hundred and sixty of the 270 preterm newborn babies that were classified as adequate for their gestational age, singletons, with birth weights below 2,500 g, and had been enrolled on the study were followed up (loss of 3.7%). Of these 260 newborn babies, 179 (68.8%) were born at the MOV/FHEMIG.

Table 1 presents some of the characteristics of the newborns, including nutritional aspects, by birth weight category. Mean calorie intake (enteral plus parenteral) above 120 kcal/kg/day is only reached after the third week of life, and the enteral diet is later the lower the birth weight. Exclusive breastfeeding predominates only until the 14th day (46.2% of the babies) and from the 21st day on, exclusive maternal breastfeeding (35.4%) associated with mixed feeding, i.e. breastmilk plus infant formula (21.1%) predominate over artificial feeding, defined here as the exclusive use of baby formulae or cow's milk *in natura* associated or not with sugar and flour (43.5%). At the end of the study, 35% of the children being monitored were on exclusive maternal breastfeeding, 18.8% on a mixture of breastmilk and baby formula, and 46.2% artificially fed.

Table 1 - Some of the characteristics of the newborns according to birth weight

	750-1,000	1,001-1,250	1,251-1,500	1,501-1,750	1,751-2,000	2,001-2,250	2,251-2,499
Number of children	9	15	40	54	47	53	42
Gestational age * (weeks)	27.0±1.3	28.6±1.7	31.4±1.3	32.4±1.5	33.3±1.3	34.4±1.4	35.4±0.9
Birth weight (g)	886.7±79.8	1,139.0±183.4	1,393.1±80.5	1,634.9±70.1	1,876.5±72.8	2,118.2±71.6	2,372.5±69.8
Percentage of male†	33.3	80.0	40.0	50.0	42.6	62.3	61.9
Length of hospital stay ‡ (days)	75.0	55.0	38.5	27.5	20.0	12.0	9.0
Fluid intake (ml) in the first week	195.9±24.7	186.3±33.3	164.9±20.5	164.6±18.7	165.8±25.9	FD	FD
Calorie intake (kcal) in the first week	66.5±7.0	73.0±19.3	86.2±17.4	87.9±16.8	88.7±26.4	FD	FD
Fluid intake (ml) in the third week	173.3±23.6	179.0±25.5	181.7±21.2	FD	FD	FD	FD
Calorie intake (kcal) in the third week	105.7±24.3	117.9±14.1	124.4±20.8	FD	FD	FD	FD
Beginning of the enteral diet (days)	5.0	5.0	3.0	2.0	1.0	1.0	1.0
Beginning of TPN (days)	3.0	3.5	4.0	4.0	5.0	5.0	4.5
Length of time of TPN (days)	14.0	11.0	6.5	7.0	8.0	6.0	5.0

TPN = total parental nutrition; FD = free demand.
* Gestational age in weeks (mean±standard deviation).
† Sex: percentage of male.
‡ Length of hospital stay in days (median).

Figure 1 shows the variation in the number of children over the study period. Observe that, in curve 1, 77.8% of the newborn babies were still being followed up at 84 days, with respect of the original number, that in curve 2, 60% remained in curve 3, 70% and in curve 4, 51.9% of the original number of newborn babies were still being monitored. In curve 5 observe that 44.7% remained in the study and that in curves 6 and 7, 56.6 and 47.6% of the newborn babies, respectively, remained.

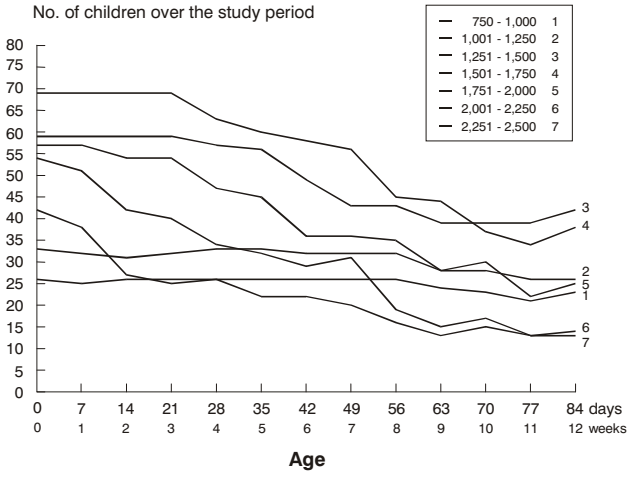

Figure 1 - Number of children followed according to birth weight

Figure 2 shows the absolute weight gain velocity (g/day) and, for all curves, there is a gradual increase in weight gain rate. The largest newborn babies (curve 6) gain practically twice as much weight as the smallest (curve 1) over the follow-up period, with weight gain at the third week being, respectively, 33.3 and 15.9 g/day for curves 6 and 1, and at week twelve, 41.4 and 22.1 g/day for the same curves.

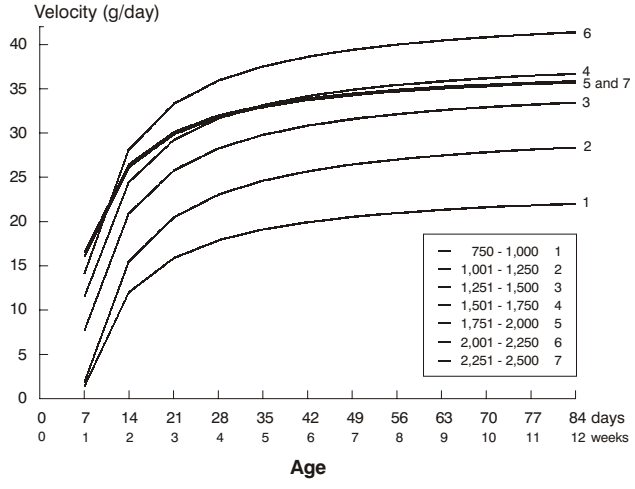

Figure 2 - Absolute weight gain velocity (g/day) of adequate for gestational age preterm newborns according to birth weight (reproduced from the Brazilian Journal of Medical and Biological Research 2003;36:761-70 with the prior authorization of its editors)

Figure 3 demonstrates the relative velocity for weight gain (g/kg/day). There is an increase in the weight gain rate from the first to the fourth week for all curves, and, from thereon, a gradual reduction, and at the twelfth week the curves tend to convergence, with very similar weight gain rates. The weight gain increment varied from 18 g/kg/day (curve 1) to 11.5 g/kg/day (curve 7) at the third week and from 10.2 g/kg/day (curve 1) to 7.5 g/kg/day (curve 7) at week twelve.

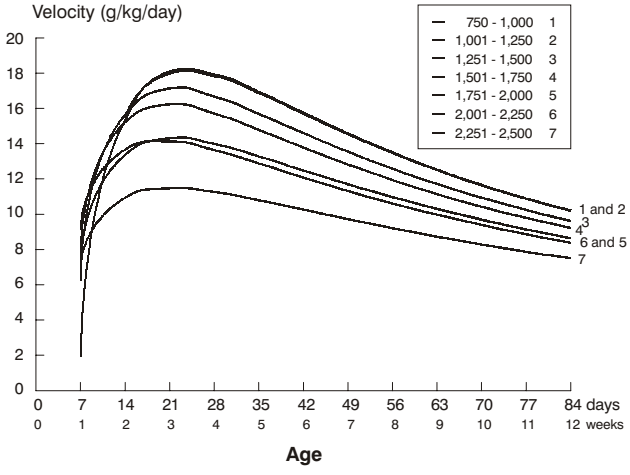

Figure 3 - Relative velocity for weight gain (g/kg/day) of preterm newborns according to weight gain (reproduced from the Brazilian Journal of Medical and Biological Research 2003;36:761-70 with the prior authorization of its editors)

The absolute velocity of head circumference increase (cm/week) is depicted in Figure 4. In curves 1, 2, 3 and 4 there is initial growth acceleration and the smaller the baby, the larger this acceleration's increment becomes. Furthermore, the head circumference growth velocity of smaller newborn babies progressively increases (curve 1 newborns have a rate of 0.55 and 0.89 cm/week, respectively, at the first and twelfth weeks). In curve 5, the rate of growth decreases gradually until week seven, from which point in maintains steady until the twelfth. The larger newborns (curves 6 and 7) exhibit a constant head circumference growth velocity, with rates of 0.62 and 0.57 cm/week, respectively.

The relative head circumference gain velocity (cm/m/week) better describes the acceleration and deceleration of head circumference growth (Figure 5). In curves 1 and 2, there is a greater head circumference increment, during the first 4 weeks of life (in curve 1, the rate increases from 2.31 to 3.14 cm/m/week and in curve 2 from 1.96 to 2.69 cm/m/week, from the first to the fourth week). In curves 3 and 4 there is also increase in head circumference, but at much slower rates. During the first week, the rates are 2.09 and 1.94 cm/m/week, respectively, and greatest head circumference rates are attained during the fourth week, values being 2.47 cm/m/week for curve 3, and 2.26 cm/m/week for curve 4. Later, all of these curves have a progressive reduction in growth rate. For curves 5, 6 and 7, head circumference growth rate, exhibits deceleration right from week one.

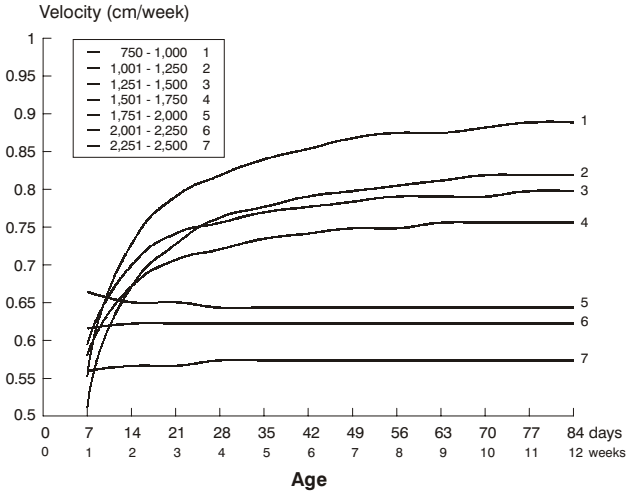

Figure 4 - Absolute velocity of head circumference increase (cm/week) of preterm newborns according to birth weight

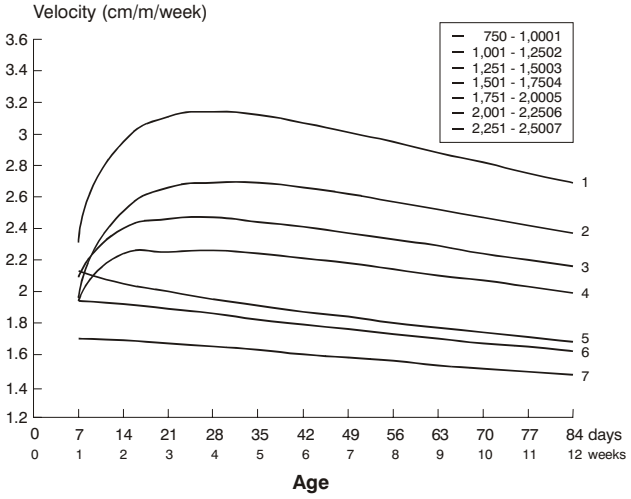

Figure 5 - Relative head circumference gain velocity (cm/m/week) of preterm newborns according to birth weight

Figure 6 represents the absolute length gain velocity (cm/week). While the smaller newborn babies (curves 1 and 2) did not exhibit faster length growth rates than did the newborn babies on the other curves, the first have greater growth velocity. Thus, the newborn babies on curve 1 who, in the first week, presented a rate of 0.04 cm/week, gradually increased this rate and reached 1 cm/week at the 12th week, and those on 2 also increased their rate from 0.25 cm/week to 0.98 cm/week from the first to the 12th week. The newborns on curves 3 and 4 who, in the first week, had a growth rate of 0.51 cm/week exhibit the highest length gain rates, achieving a rate of 1.1 cm/week by the 12th week. The larger babies (curve 5 and 6) present a discrete increase in length gain rate. Those newborns on 5, exhibited first-week values of 0.71 cm/week, increasing to 0.99 cm/week by the 12th week, while those on curve 6 increased from 0.89 to 0.99 cm/week, from the first to the 12th week. The newborn babies on curve 7 had an initial deceleration, and the rate of 1 cm/week at week one dropped to 0.9 cm/week in the 12th week. Count's model shows the increase in means between the third and seventh day as a deceleration.

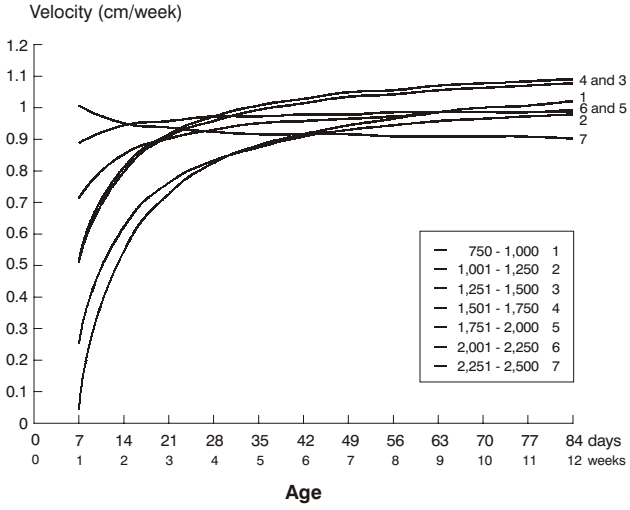

Figure 6 - Absolute length gain velocity (cm/week) of preterm newborns according to birthweight

The relative length gain velocity in cm/m/week (Figure 7) demonstrates more clearly how length growth occurs. The lower weight newborn babies (curves 1, 2, 3 and 4) exhibited greater length gain, during the first 5 weeks of life, with a progressive deceleration of the rate thereafter. The larger babies, (curves 5, 6 and 7) progressed with a diminishing length growth velocity, with the heavier the birth weight the earlier the reduction. Thus, the newborns on curve 1 accelerated their growth from the first (0.13 cm/m/week) until the seventh week of life (2.42 cm/m/week) and thereafter reduced the velocity of length growth. Curves 2, 3 and 4 progressed in a very similar manner, with curve 3 overtaking curve 2, and this last, from the sixth week on, follows curve 4 very closely. The rate of velocity, during the first week, is 0.66 cm/m/week, 1.27 cm/m/week and 1.24 cm/m/week, respectively, for curves 2, 3 and 4, with newborn babies on curve 2 attaining maximum velocity between the sixth and seventh weeks (2.20 cm/m/week), and those on curves 3 and 4 peaking between the fifth and sixth weeks, with rates of 2.29 cm/m/week and 2.23 cm/m/week, respectively. On curve 5, the increment in the length rate is 1.65 cm/m/week to 2.03 cm/m/week, from the first to the fourth week of life. Curves 6 and 7, from the first week on, present a deceleration in growth velocity.

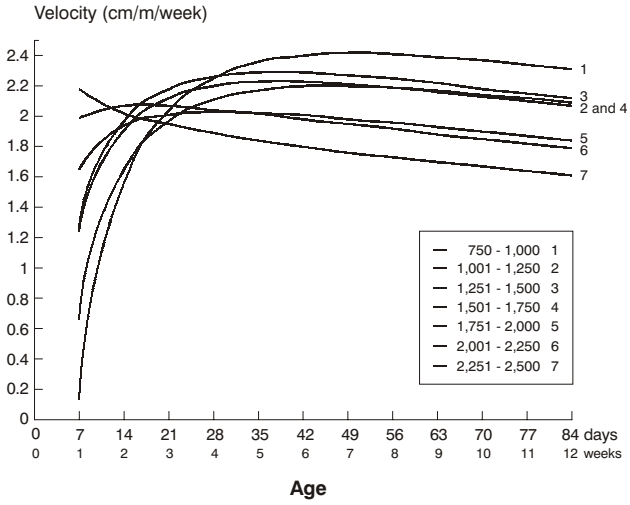

Figure 7 - Relative length gain velocity in cm/m/week of preterm newborns according to birth weight

Growth dynamics can also be evaluated taking into account both the relative velocity and somatic growth curves in relation to corrected gestational age. On curve 1, the mean gestational age is 28 weeks, on curve 2, 31 weeks, on curve 3, 32 weeks, on curve 4, 33 weeks, on curves 5 and 6, 34 weeks and on curve 7, 35 weeks. Observe, in Figure 8, that the newborn babies with the lowest weights exhibited the greatest rates of weight gain and that there is a tendency for them to approach and catch up the weight of the larger neonates. Figure 9 makes clear that the newborn babies of lowest gestational age have the greatest head circumference growth velocity, and even present peak velocity. Also observe, from the angle of curve 1, that the babies of lowest gestational age tend to attain the head circumference of those with greater gestational age. This growth dynamic observed with weight and head circumference growth is not repeated with length (Figure 10). Observe that the newborns of lower gestational age remain smaller.

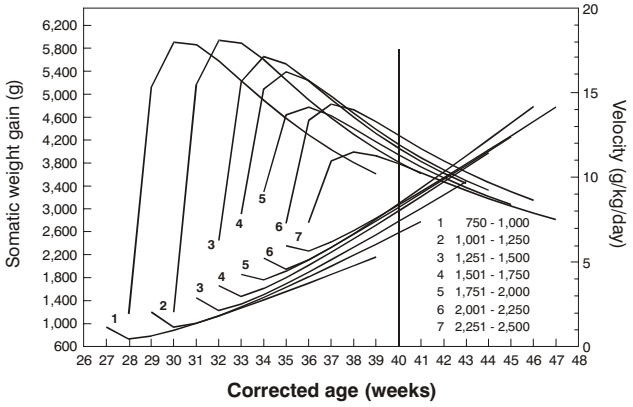

Figure 8 - Weight growth dynamics of preterm newborns: somatic growth and velocity regarding the corrected age (reproduced from the Brazilian Journal of Medical and Biological Research (2003;36:761-70) with the prior authorization of its editors)

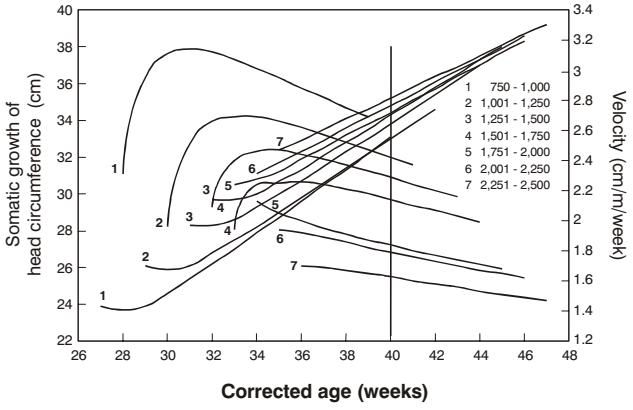

Figure 9 - Head circumference growth dynamics of preterm newborns: somatic growth and velocity regarding the corrected age

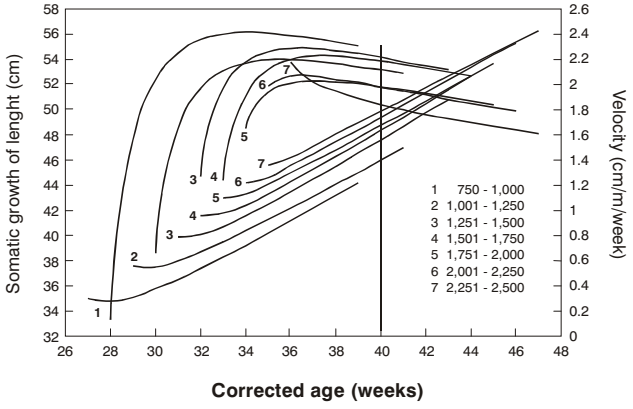

Figure 10 - Length growth dynamics of preterm newborns: somatic growth and velocity regarding the corrected age

Discussion

Little is known about the postnatal growth dynamics of preterm newborn babies, as evaluated by velocity curves. The majority of papers of growth in relation to birth weight[14-24] do not include velocity curves. Nevertheless, such curves are important since they permit a better understanding of the accelerated and normal growing phases of premature infants than do simple values expressed in g/day (cm/week) or g/kg/day (cm/m/week).

During the accelerated growth phase, analyzing absolute velocity (Figure 2), all curves exhibit an acceleration in weight gain from the first to the second and from the second to third weeks. It is, however, when relative velocity is analyzed (Figure 3), which includes the rate at which weight is incorporated, that the capacity of neonates, primarily those with lower weights, have to catch up on their growth deficits becomes clear. There is acceleration of the rate of weight increase during the first 4 weeks of life for all curves, the period during which peak velocity occurs, achieving the highest rates of weight increase.

Later, the babies achieve normal growth velocity, depending on their growth path. There is a progressive increase in weight gain in g/day (Figure 2), which is directly proportional to birth weight, until the seventh week, when weight gain becomes more stable. With time, the difference in weight gain reduces, although the largest newborn babies present the highest rates. It is possible that the reduction in the difference between the mean weight gains (g/day) of the different categories is a result of the fact that the smaller newborns accelerate their growth, which becomes obvious when relative velocity is analyzed (g/kg/day). Average weight increase velocities in g/kg/day (Figure 3) are inversely proportional to birth weight, being higher among those newborn babies of lower weight. From the sixth week onwards, there is a deceleration in rates of weight increase, with the values of these rates drawing together at the end of the study (12th week), probably translating into smaller newborns, after a period of acceleration catching up and maintaining a growth rate similar to that of the larger ones.[6,25-27]

The analysis of the rate of head circumference increase, both in cm/week (Figure 4) and in cm/m/week (Figure 5) is very similar. In both the increase in head circumference is inversely proportional to birth weight, i.e. the smaller the weight, the greater the increase in head circumference. The newborn babies on curves 1, 2, 3, and 4 (gestational ages of 27, 29, 31 and 32 weeks, respectively), present increases in head circumference, during the first 4 weeks, the phase of greatest growth acceleration. Furthermore, while they continue to exhibit an increase in head circumference growth, this increase reduces progressively, after maximum acceleration. On curve 5, the mean gestational age is 34 weeks, and on curves 6 and 7 it is 35 weeks and during this period of the study only the deceleration phase of head circumference growth is evident. With respect of head circumference growth velocity, there is an increase in head circumference velocity for the smaller newborn babies until a peak is reached, from which there is a gradual reduction

in velocity, although there are differences of opinion over the timing of this peak and whether it varies or not with gestational age.[25,28,29]

For length, it is only with relative velocity (Figure 7) that it can be observed that length gain (cm/m/week) is inversely proportional to birth weight. The length rate curves 1, 2, 3 and 4 increase until the fourth and fifth weeks, and, after a period of constant values, begin to drop off, and at the end of the study these curves tend to run together. Curve 1, with lowest gestational age, presents the highest growth velocity. On curves 5 and 6 there is a small increase in length, followed by deceleration of growth and, on curve 7, growth velocity reduces from week one on, probably as a result of the older gestational ages. Brandt[25] reports that after peak length growth velocity, rates are constant and growth occurs with a constant reduction in rate.

While velocity curves remain little used in clinical practice, they hold important information, primarily on relative velocity. The rates of weight, head circumference and length incorporation appear to be closer to an analysis of growth dynamics, demonstrating to what extent smaller newborn babies exhibit greater growth velocity in relation to the largest and tend to catch them up, agreeing with published literature,[6,25-27] which may not be perceptible using somatic growth curves or absolute velocity curves (g/day).

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Corresponding author:
Lêni Márcia Anchieta
Rua Tupis, 426/1104
CEP 30190-060 - Belo Horizonte, MG
Brazil
Phone: +55 (31) 3222.1524
E-mail: lenima@terra.com.br