Chapter

Characteristics of Catch-Up Growth in Very Low Birth Weight Infants (<1500 g)

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Abstract

Features of catch-up growth are not well established in very low birth weight infants (VLBW). The aim of this study is to analyze the catch-up growth in height and some factors associated in a cohort of VLBW (<1500 g) from birth to age 14 years. Retrospective registration of weight and height at birth and ages 0.5, 1, 2, 3, 4, 6, 8, 10, 12 and 14 years in a cohort of 170 VLBW have been recorded Anthropometric variables were compared with those from a control group. Sixty-nine (40.6%) were small for gestational age (SGA subgroup) and 101 (59.4%) were appropriate for gestational age (AGA subgroup). Thirty-seven (21.8%) were extremely low birth weight (ELBW), and 32 (18.8%) extremely preterm (EPT). At age 2, 4 and 10 years, 49.4%, 78.9% and 87.1% VLBW, respectively, did reach normal height. Between 4 and 10 years of age, only 8.2% of VLBW reached normal height. At 10 years of age, 7% of VLBW (1000–1500 g) and 35% of ELBW (<1500 g) showed short stature ($p = 0.001$). Almost the entire sample of VLBW with normal height at age 2, 4 and 10 have reached an adequate catch-up growth in weight in the previous evaluations. ELBW, SGA and EPT were found to be independent predictors for inadequate catch-up growth in height at 2, 4, and 10 years of age. The growth pattern of children born preterm has particular features: they have a lower rate and/or slowness in the catch-up growth in height with respect to that described in full-term small-for-gestational-age infants. Catch-up in weight appears to be a decisive factor for catch-up in height, and, on this basis, we recommend a rigorous nutritional follow-up in these individuals. If these measures do not help improve catch-up in height, they may be eligible for the establishment of rhGH therapy.

Keywords: Catch-up growth, Extremely low birth weight, Growth pattern, Intrauterine growth retardation, Preterm infant, Very low birth weight infant

1. Introduction

Full-term infants who present with intrauterine growth restriction constitute a varied group with multifactorial conditions. These infants, along with high rates of perinatal morbidity and mortality, undergo an increased risk of cardiovascular and/or metabolic disease in adult life [1]. They subsequently experience an accelerated compensating growth, known as catch-up growth, which usually ceases at age 2 [2–4]. As a matter of fact, those children whose catch-up is inadequate have low chance to reach a normal size in adult life; that is one of the approved indications for the treatment with recombinant growth hormone [5–8].

Nevertheless, the features of catch-up growth are not well characterized in very preterm infants (<32 weeks of gestation) or very low birth weight infants (<1.500 g). In accordance with current knowledge, there is evidence that supports the need to experience adequate extrauterine growth in order to acquire optimal development of all their organic capacities. The increased survival rate of very low birth weight infants (<1500 g) at present time, as a consequence of the recent advances in obstetric and perinatal care, entails a higher risk of sensorineural morbidity and/or disability [5, 9, 10]. In any case, the follow-up of these patients, even though there is no actual consensus, suggests that this catch-up could extend to a later stage, and so condition the prognosis of adult size [11–18].

Catch-up is defined as a fast paced growth after a period of growth failure whose aim is to approach to the measurements of normal term-born infants [2–4]. When this event fails to develop during the initial stages of life, neurological deficits like behavioral difficulties and neurocognitive deficits in very preterm infants are likely to be found [19–21]. In addition, correlations between rapid and early growth (especially of weight) in preterm-born infants and the progression to metabolic syndrome in adulthood have been reported [19, 22, 23]. There is still poor understanding on the factors that determine when catch-up growth occurs in very preterm infants or very low birth weight infants, but it is well-known that low birth weight, early gestational age and medical complications have a particularly negative effect on postnatal growth [16]. In addition, the catch-up growth in weight in these children, which presents simultaneously to catch-up growth in length, has been less frequently studied, even though it has been proved that caloric intake has a positive impact on postnatal growth in preterm infants [24–27].

The main aim of the work is to perform a longitudinal descriptive study of anthropometric measurements in a group of very low birth weight (VLBW) infants, aged from birth to 14 years of age, and to analyze the features of catch-up growth in height and some of the factors associated in these children.

2. Methods

There is a specific program in our region (Comunidad Foral de Navarra), fostered by the Regional Health Service, that intends to promote healthy lifestyle and monitors child growth and development. By means of periodic consultation (usually at birth and during the first year, and ages 0.5, 1, 2, 3, 4, 6, 8, 10, 12 and 14 years), the program accomplish the registration of anthropometric measurements (weight and height) and saves different data in the clinical records.

These children, who represent a cohort of VLBW infants (<1500 g), have been evaluated by a pediatrician and/or pediatric nurse by the use of the different facilities available (our public Health Service guarantees universal accessibility in distance and personal assistance). The different consultations were programmed at birth and ages 0.5, 1, 2, 3, 4, 6, 8, 10, 12 and 14 years. A brief medical history, basic physical exam and the anthropometric measurements (weight and height) were recorded. The only requirements to be included were a Caucasian origin from Spanish parents, and the birth place (the Neonatal Unit of the Navarra Hospital Complex in Pamplona, Spain, which is the reference Hospital) in the period January, 2001-December, 2005.

Body measurements (weight and height) were taken during physical exam in underwear and barefoot. We used an Año-Sayol scale (reading interval 0 to 120 kg and a precision of 100 g) for the measurement of weight and a Holtain wall stadiometer (reading interval 60 to 210 cm, precision 0.1 cm) for the measurement of height.

We collected a sample of 217 births of babies who met the criteria of VLBW, 47 of whom were excluded due to different reasons: perinatal mortality in 20 (9.2%), the finding of severe malformations or chromosomopathies in 6 (2.8%), severe neurosensory disability and motor sequelae in 5 (2.3%), ethnic origin in 8 (3.7%) and other reasons (geographical distance to hospital and difficulties for transportation, absence of continuity in the evaluations of the pediatric health screening, etc.) in 8 cases (3.7%).

The children (VLBW) in this cohort were divided in two subgroups: newborn infants who were appropriate for gestational age (AGA subgroup) and newborn infants who were small for gestational age (SGA subgroup). The difference between both groups was that birth weight and/or length were higher or equal/lower than two standard deviations below the average of a reference population for gestational age and sex, respectively. We used the growth reference charts for newborns from the anthropometric growth patterns of preterm from Carrascosa et al. [28]. In addition, when birth weight was lower than 1.000 g they were defined as extremely low birth weight (ELBW). Another way to classify newborns was based on gestational age: extremely preterm (EPT) when gestational age was lower than 28 weeks, very preterm (VPT) when gestational age was between 28–32 weeks, and late preterm (LPT) when gestational age was between 32–37 weeks.

A control group was established by recruiting children from a different observational epidemiological study made of an infant population (healthy full-term infants, Caucasian and children from Caucasian parents); the periodic evaluations followed the same patterns as those for VLBW infants (482 boys and 448 girls) [29].

An adequate catch-up growth in height or weight was defined when height or weight in VLBW infants, respectively, surpassed the value of 2 standard deviations below the mean in the growth charts of the control group [2–4].

3. Statistical analysis

Results are presented in the successive tables as percentages (%) and means (M) with corresponding standard deviations (s.d.) and confidence intervals (95% CI). The statistical analysis (descriptive statistics, Student's t-test, analysis of variance, Chi-square and multiple logistic regression analysis) was executed with the program *Statistical Packages for the Social Sciences* version 20.0 (Chicago, IL, USA). The statistical significance was reached with a P-value of 0.05.

This study was submitted and subsequently approved by the Ethics Committee for Human Investigation of the Navarra Hospital Complex, Pamplona, Spain (in compliance with the ethical standards of the 1964 Declaration of Hensinki and later amendments). Parents and/or legal guardians were aware of the characteristics and requirements of the study and provided acceptance for the participation in all cases.

4. Results

The sample of VLBW infants who have been recruited for this study consists of 170 children (82 boys and 88 girls). In the aggregate, 40.6% (n = 69) of the infants were included as small for gestational age (SGA subgroup) and the remaining 59.4%

(n = 101) as appropriate for gestational age (AGA subgroup). In the SGA subgroup, 59.4% (n = 41) of children had a history of weight and height alterations at birth, while specific alterations of height (23.2%, n = 16) or weight (17.4%, n = 12) were less frequent (**Figure 1**).

Multiple pregnancies amount to 42.4% (n = 72), being twin pregnancies predominant, (**Figure 2**).

On the basis of gestational age, they have been subdivided into extremely preterm (n = 32, 18.8%), very preterm (n = 72, 42.4%) and late preterm (n = 66, 38.8%) (**Figure 3**). Thirty-seven (21.8%) infants were included as ELBW.

Table 1 exposes and compares the values of the anthropometric measurements at birth of VLBW infants in the AGA and SGA subgroups and classified by sex. We do not appreciate statistically significant differences in the mean weight and height values at birth between the two groups. The values of gestational age were significantly higher in the SGA subgroup than in the AGA subgroup.

Table 2 displays and compares the mean values for height, weight and growth rate in VLBW infants and the control group from birth to 10 years of age. Figures for height and weight were significantly lower in VLBW than in the control group. In contrast, growth rate in the first two years of life in was significantly higher in VLBW infants than in the individuals of the control group.

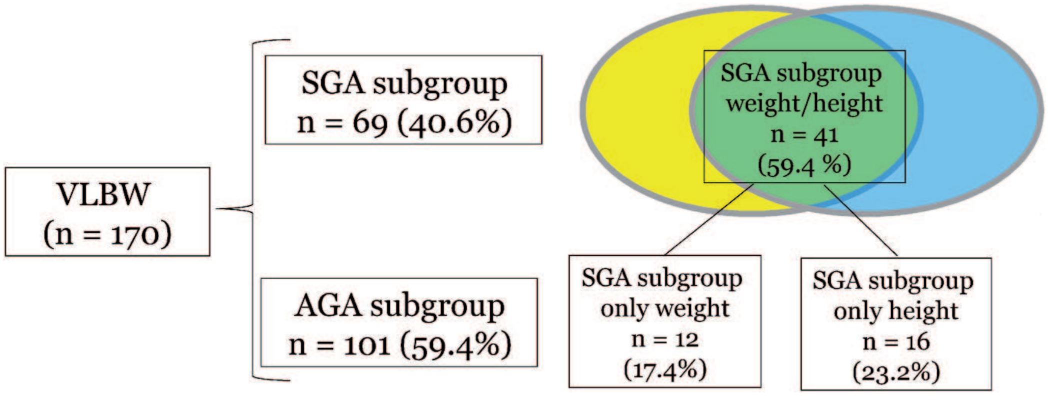

Figure 1.
Classification of VLBW according to weight and/or height at birth.

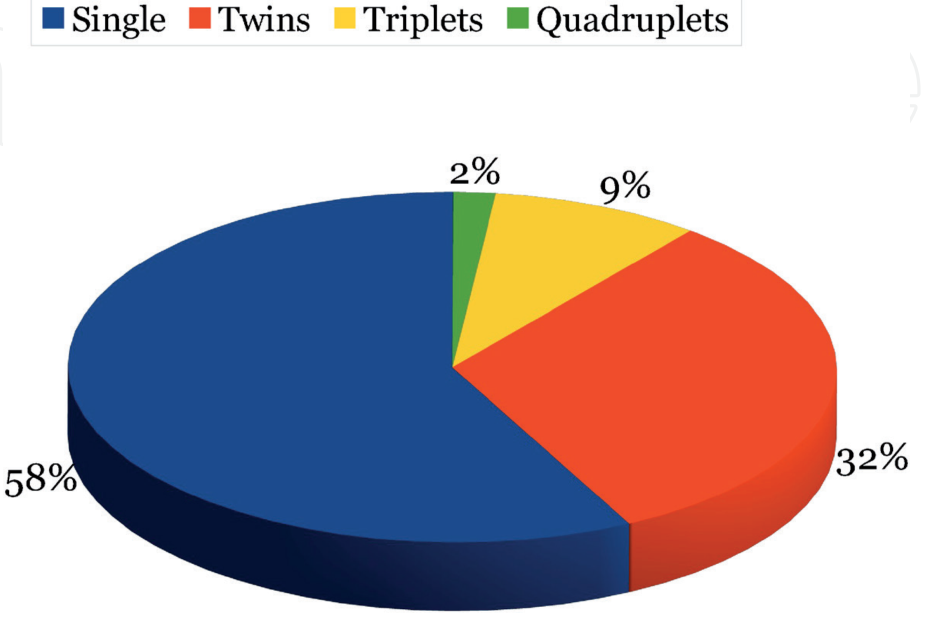

Figure 2.
Distribution of VLBW according to the type of pregnancy.

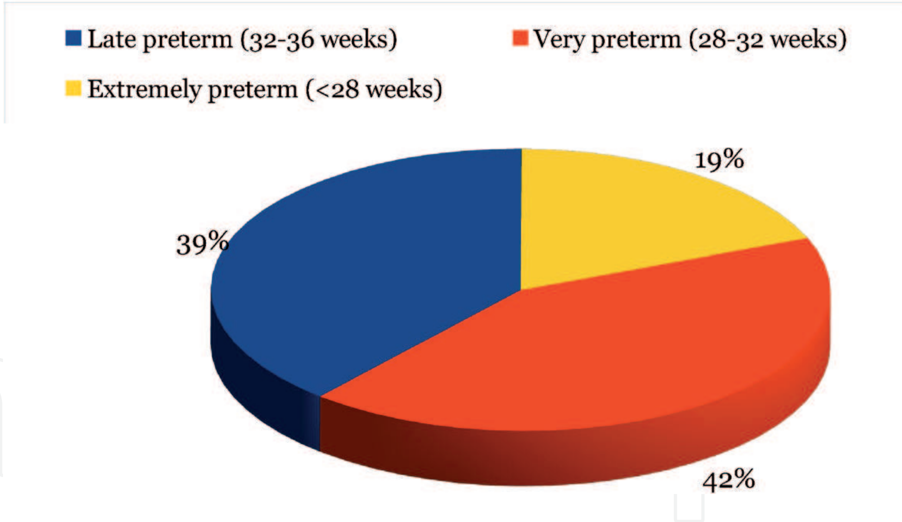

Figure 3.
Distribution of VLBW according to the degree of prematurity.

	Boys		Girls	
	AGA subgroup (n = 52)	**SGA subgroup (n = 30)**	**AGA subgroup (n = 49)**	**SGA subgroup (n = 39)**
Gestational age* (weeks)	28.7 ± 1.9	33.3 ± 1.9	28.9 ± 2.1	32.6 ± 3.1
Weight (g)	1204.3 ± 222.8	1257.4 ± 179.9	1145.8 ± 229.7	1134.0 ± 256.5
Height (cm)	38.3 ± 3.1	39.0 ± 2.4	38.2 ± 2.6	37.4 ± 3.5

**Student's t-test, p < 0.05 among AGA and SGA.*
AGA: appropriate for gestational age. SGA: small weight for gestational age.

Table 1.
Gestational age, weight and height data from VLBW infants at birth in both sexes (M ± SD).

Figure 4 shows the percentage of VLBW infants who reached normal height at the different stages that were evaluated in the study. At age 2, 4 and 10 years, 49.4%, 78.9% and 87.1%of infants, respectively, had gained normal height. In this sense, 8.2% of VLBW infants presented with normal height between ages 4 and 10 years.

The analysis reveals that 86% of VLBW infants that had gained normal weight after the first year of life reached normal height ($P < 0.001$) by age 2 years. Additionally, 98.6% of VLBW infants with normal weight at age 2 had reached normal height ($P < 0.001$) by age 4. In the same way, 97.2% of VLBW infants with normal weight at age 4 appear with normal values for height ($P < 0.001$) by age 10, 99.2% of VLBW infants with normal weight at age 6 showed normal values for height by age 8 ($P < 0.001$), and finally, all VLBW infants that presented with normal weight at age 10 had also normal height at this age ($P < 0.001$).

Table 3 states the comparison of mean values for height, weight and growth rate between AGA y SGA subgroups from birth to 10 years of age. The AGA subgroup features significantly higher values for height with respect to SGA subgroup at age 1, 2, 3, 4 and 6, as well as higher values for weight at age 1, 2, 3 and 6. There were no statistically significant differences in growth rate between both groups in every stage evaluated.

Figure 5 shows the figures of the percentages of infants in the AGA and SGA subgroups that gained normal size at the different stages under assessment. There were no statistically significant differences between the groups, except at age 10:

Height (cm)			
Age (years)	**VLBW group**	**Control group**	**p-value**
0	38.2 ± 3.3	50.0 ± 2.0	<0.001
6 mo	60.2 ± 3.5	67.2 ± 2.2	<0.001
1	70.9 ± 3.4	75.9 ± 2.7	<0.001
2	83.8 ± 4.0	88.1 ± 3.1	<0.001
3	92.5 ± 4.2	96.5 ± 3.4	<0.001
4	100.2 ± 4.9	104.0 ± 4.2	<0.001
6	113.8 ± 5.6	117.3 ± 4.8	<0.001
8	125.6 ± 6.0	129.6 ± 5.4	<0.001
10	136.2 ± 6.9	140.7 ± 6.2	<0.001
Weight (kg)			
Age (years)	**VLBW group**	**Control group**	**p-value**
0	1.2 ± 0.2	3.3 ± 0.4	<0.001
6 mo	5.7 ± 1.0	7.7 ± 0.8	<0.001
1	8.0 ± 1.2	10.0 ± 1.2	<0.001
2	10.5 ± 1.5	12.7 ± 1.4	<0.001
3	12.7 ± 2.0	15.2 ± 1.8	<0.001
4	14.8 ± 2.5	17.6 ± 2.4	<0.001
6	19.5 ± 3.5	22.7 ± 3.6	<0.001
8	25.0 ± 5.4	29.6 ± 5.6	<0.001
10	31.5 ± 8.1	37.2 ± 7.4	<0.001
Velocity height (cm/y)			
Age (years)	**VLBW group**	**Control group**	**p-value**
0–6 mo	44.1 ± 4.9	34.0 ± 6.5	<0.001
0–12 mo	32.6 ± 3.1	26.0 ± 2.6	<0.001
1–2	12.9 ± 1.8	11.9 ± 2.4	<0.001
2–3	8.8 ± 2.2	8.4 ± 1.9	0.060
3–4	7.5 ± 1.9	7.7 ± 1.8	0.190
4–6	6.6 ± 1.4	6.7 ± 1.0	0.895
6–8	6.1 ± 1.1	6.1 ± 1.1	0.453
8–10	5.5 ± 1.3	5.6 ± 1.3	0.558

VLBW: very low birth weight.

Table 2.
Changes in the values of height, weight and growth rate of VLBW and control group (M ± SD).

17% of children in the SGA subgroup (n = 12) and 10% of children in the AGA subgroup (n = 10) presented with low height values (P = 0.018).

Table 4 describes the mean values for height, weight and growth rate in ELBW (<1000 g) and VLBW (1001–1500 g) infants from birth to 10 years. Mean values for weight and height were significantly lower in ELBW than in VLBW in every age considered except for 10 years. There were no significant differences in growth rate between both groups in any period of age.

Figure 6 presents the percentages of VLBW (1000–1500 g; n = 133) and ELBW (<1000 g; n = 37) infants that reached normal height at the different ages under assessment. There were significant differences between groups at every age evaluated. In this way, 7% of VLBW infants (n = 9) and 35% of ELBW infants (n = 13) showed short stature (P = 0.001) at age 10.

In the SGA subgroup, 7 out of the 12 children that presented with short stature at age 10 (7 of whom were ELBW) had reached normal values in height by age 14 (6 of them had taken treatment with recombinant human growth hormone [rhGH]); the remaining 5 (3 of whom were ELBW) maintained short stature (3 of them had treatment with rhGH). Treatment with rhGH was started between ages 6.5

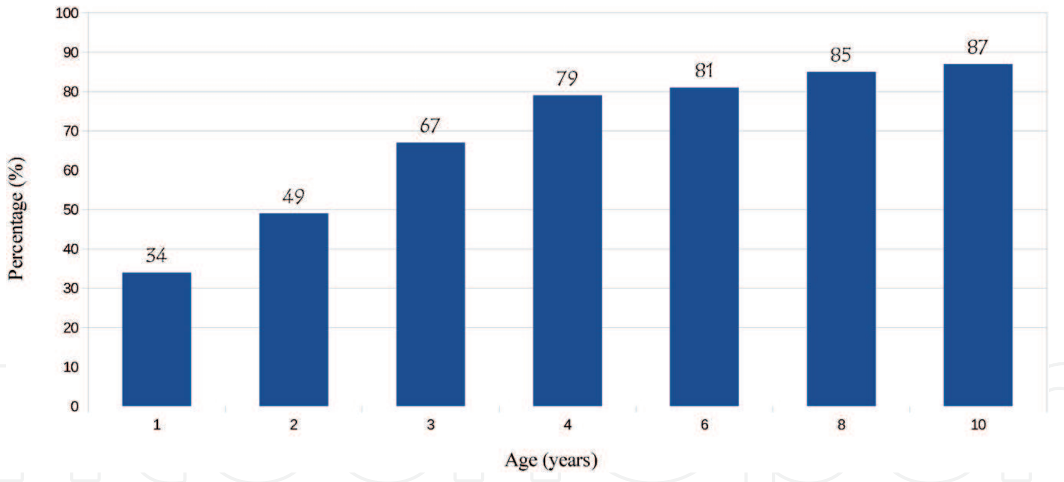

Figure 4.
Percentages of adequate catch-up growth in height in VLBW infants.

Height (cm)			
Age (years)	**SGA subgroup**	**AGA subgroup**	**p-value**
0	38.1 ± 3.8	38.2 ± 2.8	0.786
6 mo	60.1 ± 4.0	60.4 ± 3.4	0.702
1	70.2 ± 3.6	71.4 ± 3.4	0.008
2	82.9 ± 3.9	84.5 ± 3.9	0.027
3	91.6 ± 3.8	93.1 ± 4.4	0.030
4	99.1 ± 4.8	100.9 ± 5.0	0.035
6	112.4 ± 6.0	114.6 ± 5.7	0.025
8	124.6 ± 5.7	126.4 ± 6.2	0.109
10	135.5 ± 6.6	137.0 ± 7.2	0.409
Weight (kg)			
Age (years)	**SGA subgroup**	**AGA subgroup**	**p-value**
0	1.2 ± 0.2	1.2 ± 0.2	0.730
6 mo	5.5 ± 1.0	5.9 ± 0.9	0.081
1	7.6 ± 1.2	8.3 ± 1.1	0.002
2	10.0 ± 1.6	10.8 ± 1.5	0.002
3	12.1 ± 1.6	13.2 ± 2.1	0.001
4	14.4 ± 2.3	14.8 ± 3.4	0.355
6	18.7 ± 3.3	19.9 ± 3.6	0.032
8	24.4 ± 5.2	25.5 ± 5.4	0.258
10	31.5 ± 8.1	31.7 ± 8.3	0.902
Velocity height (cm/y)			
Age (years)	**SGA subgroup**	**AGA subgroup**	**p-value**
0–6 mo	44.5 ± 5.4	43.9 ± 4.4	0.511
6–12 mo	20.3 ± 4.0	21.9 ± 4.6	0.068
0–12 mo	32.2 ± 3.4	33.0 ± 2.8	0.170
1–2	12.8 ± 1.5	13.1 ± 2.1	0.423
2–3	8.6 ± 2.1	8.9 ± 2.2	0.553
3–4	7.4 ± 2.0	7.6 ± 1.7	0.650
4–6	6.4 ± 1.3	6.7 ± 1.4	0.225
6–8	6.1 ± 1.3	6.2 ± 1.0	0.678
8–10	5.4 ± 1.2	5.5 ± 1.5	0.750

AGA: appropriate for gestational age. SGA: small weight for gestational age.

Table 3.
Changes in the values of height, weight and growth rate of VLBW (AGA and SGA subgroups. (M ± SD).

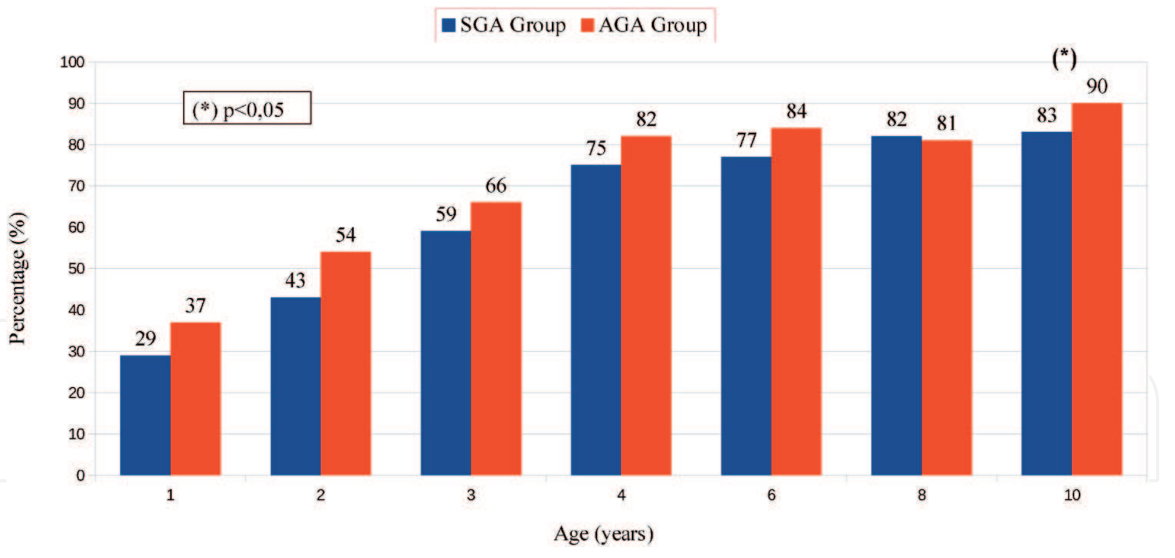

Figure 5.
Percentages of adequate catch-up growth in height in AGA and SGA groups (chi-square).

Height (cm)			
Age (years)	**ELBW group (<1000 g)**	**VLBW group (1000–1500 g)**	**p-value**
0	33.6 ± 2.7	39.4 ± 2.1	<0.001
6 mo	55.8 ± 2.8	61.4 ± 2.7	<0.001
1	67.0 ± 2.8	71.8 ± 2.8	<0.001
2	75.9 ± 3.9	84.8 ± 3.2	<0.001
3	79,7 ± 4.2	93.5 ± 3.5	<0.001
4	96.4 ± 5.9	101.1 ± 4.1	<0.001
6	110.5 ± 6.1	114.5 ± 5.2	<0.001
8	121.1 ± 6.8	126.8 ± 5.3	<0.001
10	133.8 ± 7.3	136.8 ± 6.7	0.179
Weight (kg)			
Age (years)	**ELBW group (<1000 g)**	**VLBW group (1000–1500 g)**	**p-value**
0	0.8 ± 0.1	1.3 ± 0.2	<0.001
6 mo	4.7 ± 0.8	6.0 ± 0.8	<0.001
1	6.8 ± 1.1	8.3 ± 1.0	<0.001
2	9.2 ± 1.3	10.9 ± 1.3	<0.001
3	11.2 ± 1.5	13.1 ± 1.8	<0.001
4	13.0 ± 2.0	15.3 ± 2.3	<0.001
6	17.1 ± 2.7	20.0 ± 3.4	<0.001
8	21.5 ± 4.1	26.1 ± 5.2	<0.00
10	32.6 ± 8.3	32.7 ± 8.3	0.048
Velocity height (cm/y)			
Age (years)	**ELBW group (<1000 g)**	**VLBW group (1000–1500 g)**	**p-value**
0–6 mo	44.9 ± 6.3	43.9 ± 4.4	0.409
6–12 mo	22.8 ± 4.5	20.8 ± 4.3	0.039
0–12 mo	33.9 ± 3.7	32.3 ± 2.9	0.065
1–2	12.7 ± 2.3	13.0 ± 1.7	0.492
2–3	9.0 ± 2.5	8.7 ± 2.1	0.621
3–4	7.4 ± 2.1	7.5 ± 1.7	0.698
4–6	6.5 ± 1.2	6.7 ± 1.3	0.595
6–8	5.8 ± 1.1	6.2 ± 1.1	0.171
8–10	5.7 ± 1.1	5.5 ± 1.3	0.530

ELBW: extremely low birth weight. VLBW: very low birth weight.

Table 4.
Changes in the values of height, weight and growth rate of VLBW (1000–1500 g) and ELBW (< 1000 g). (M ± SD).

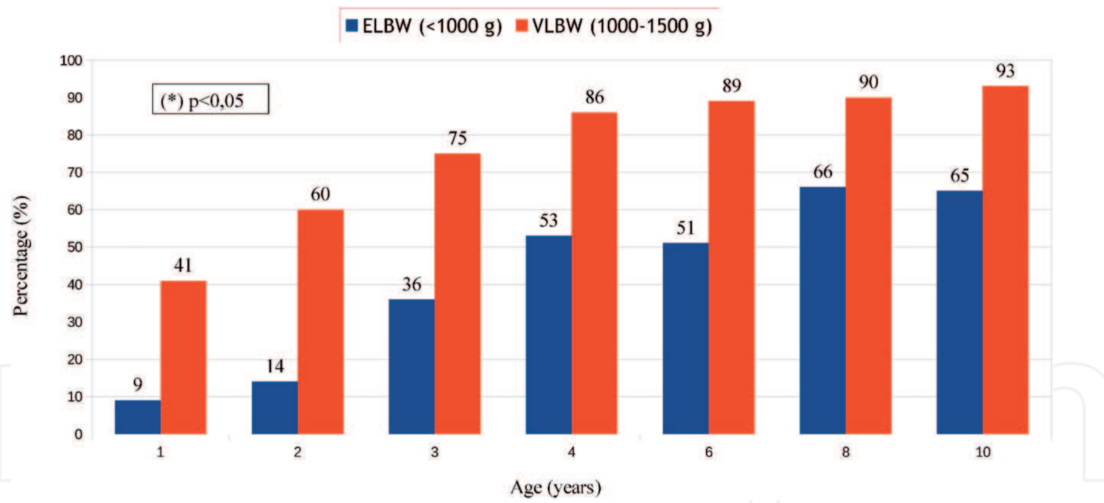

Figure 6.
Percentages of adequate catch-up growth in height in ELBW and VLBW infants (chi-square).

Items	Inadequate catch-up growth in height		
	At 2 years OR (95% CI) P-value	At 4 years OR (95% CI) P-value	At 10 years OR (95% CI) P-value
Birth weight VLBW (1000–1500 g), n = 133 ELBW (<1000 g), n = 37	Referent 8,9 (3.3–24.5) 0.001	Referent 5,9 (3.6–13.6) 0.001	Referent 5.3 (2.1–13.4) 0.001
AGA group, n = 69 SGA group (weight/height), n = 41	Referent 1,6 (0,8–2.9) 0,150	Referent 1,5 (0.7–3.1) 0,300	Referent 2.6 (1.1–6.4) 0.038
AGA group, n = 69 SGA group (only weight), n = 12	Referent 1.4 (0.7–2.7) 0.291	Referent 1.3 (0.6–2.9) 0.457	Referent 2.3 (0.9–5.5) 0.069
AGA group, n = 69 SGA group (only height), n = 16	Referent 2.0 (1.3–1.7) 0.048	Referent 1.9 (1.2–4.0) 0.033	Referent 2.8 (1.1–6.8) 0.024
Gestation type Single, n = 98 Multiple, n = 72	Referent 0,9 (0.5–1.5) 0.620	Referent 0.9 (0.4–1.9) 0.862	Referent 1.4 (0.6–3.6) 0.431
Gestational age 32–37 weeks (LPT), n = 66 <28 weeks (VPT), n = 72 28–32 weeks (EPT), n = 32	Referent 2.5(1.1–5.9) 0.035 2.6 (1.1.6.4) 0.033	Referent 7.2(2.6–19.8) 0.001 4.2 (1.6–10.8) 0.003	Referent 4.5(1.3–14.9) 0.015 1.9 (0.7–5.3) 0.242

VLBW: very low birth weight. ELBW: extremely low birth weight. AGA: appropriate for gestational age. SGA: small weight for gestational age. LPT: late preterm. VPT: very preterm. EPT: extremely preterm.

Table 5.
Logistic regression analysis of factors associated with inadequate catch-up growth.

and 8.3 years. In the AGA subgroup, 2 of the 10 children that presented with short stature at age 10 (7 of whom were ELBW) had reached a normal height at 14 years (1 of them had received rhGH therapy at age 8.9 years) and 8 (6 of them ELBW) kept in short stature (1 of them started rhGH therapy at age 7.8 years, and 7 of them were not entitled to receive treatment due to normal responses in growth hormone stimulation tests).

Table 5 displays the results of the multiple logistic regression analysis conducted to study the association of neonatal clinical history with inappropriate catch-up growth in height at ages 2, 4, and 10. The analysis shows that the conditions of ELBW, SGA for height and preterm birth before 28 weeks of gestation were associated with inadequate catch-up growth in height at 2, 4, and 10 years. On the other side, SGA for both weight and height was associated with inadequate catch-up growth only at age 10, whereas preterm birth between 28 to 32 weeks of gestation was associated with inadequate catch-up growth only at ages 2 and 4. Additionally, multiple birth was not associated with inadequate catch-up growth at ages 2, 4 or 10 years.

5. Discussion

The terms “intrauterine growth restriction” (IUGR) and “small for gestational age” (SGA) newborn are not strictly equivalent concepts [30], since they are related to different chronological stages (fetal growth and anthropometric measurements at birth, respectively). Nevertheless, they refer to failure to reach the genetic growth potencial during the prenatal period as an adaptive response to an adverse uterine environment. In any way, both terms are used indistinctly in daily clinical practice in order to cluster those newborns whose weight and/or height at birth are equal to/below 2 standard deviations under the average of a reference population on the basis of gestational age and sex. In this case, the majority of children included in the so-called SGA group presented with a combined alteration in weight and height, whilst the proportion of children with exclusive weight or height disorder was slightly lower.

This definition requires a precise diagnosis of gestational age and the registration of anthropometric measurements after birth, whose values should be contrasted with reference standards for gestational age and sex. The choice of reference patterns is a determining factor in the assessment of newborn growth [31]. In fact, the variability of the anthropometric variables in relation to racial, genetic, social, environmental and maternal lifestyle factors make it advisable to use local or national growth reference charts. The charts from Lubchenco et al. [32], which were published in the 60s, have been widely used and are characterized by a contrasted clinical utility. At present, the most qualified local (Spanish) reference charts, which have been used in the present study, are the newborn (26–42 weeks of gestational age) weight and height charts from the anthropometric growth patterns of preterm from Carrascosa et al. [28].

Fetal development and intrauterine growth are complex processes in which continuous and harmonious cellular proliferation and differentiation take place. Multiple factors (maternal, fetal, placental and environmental) have been mentioned to have a negative impact on the fetus and set off a series of functional and structural adaptive changes that conclude in fetal growth restriction (in the so-called “thrifty phenotype hypothesis”). They are linked to different changes in hormone sensitivity and/or secretion that entails an increased risk of developing metabolic and/or endocrine disorders in adult life [33, 34]. In any way, most term newborns with previous intrauterine growth restriction manifest a compensatory growth (catch-up growth) after birth, mainly in the first year of life, that enables approximately 90% of the individuals to surpass the threshold of 2 SDs under the average in the reference population, or, in other words, to get normal height [2–4]. Even so, whenever this compensatory growth does not occur, a normal final height in adulthood is not likely to be reached. By knowing so, this event is considered one of the indications for rhGH therapy approved by the United States Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Growth Hormone Research Society, with the intention to boost the initial compensatory growth and/or to keep normal growth velocity [3, 35, 36].

The recent advances in obstetric and perinatal care have led to a considerable decrease in VLBW infants mortality; despite this, and owing to the potential sensorineural morbidity in this children, these patients are usually enlisted in follow-up programmes whose goal is the early detection of neurodevelopmental problems [1, 37]. The improvement of these programmes has eased the standardization of dietary and nutritional advices, and enabled growth monitoring in the first years of life. It also facilitates the analysis, as we performed in this study, of the evolution of anthropometric variables in VLBW infants [38].

The results obtained in this study confirm that, on one side, the VLBW newborns undergo a postnatal compensatory growth that is maximum during the first year of life, as it occurs in term newborns that are SGA. As a matter of fact, growth velocity during the first 12 months of life in VLBW was considerably higher than in the control group; this explains, to a great extent, the noticeably proportion of individuals in this group that reach normal height by age 2 years [39]. On the other side, this study remarks that VLBW infants have a lower rate and/or delay in the catch-up growth in height when comparing to that observed in full-term SGA infants [4, 16–18, 24, 25]. In point of fact, 50.6%, 21.1% and 12.9% of individuals, maintained short stature at age 2, 4 and 10, respectively; in other words, these individuals reached normal height in a similar percentage than that for full-term SGA infants at age 2. Additionally, barely 8.2% of children reached normal height between ages 4 to 10. Despite current data are inconsistent, these results are somehow congruent with those exposed by the different authors that previously noticed that catch-up in VLBW infants could be delayed [12, 15, 40–44]. Nevertheless, none of the authors cited has screened the influence of catch-up growth in weight, which is concurrent with the catch-up in height and, in accordance to the data collected, plays a decisive role [24, 25]. In effect, a great majority of individuals who present with normal height at age 2, 4 and 10 have gained an adequate catch-up growth in weight in the previous evaluations. For this reason, these individuals should follow a strict nutritional control in order to raise an issue on the prescription of nutritional supplements with the challenge to get weight recovery as fast as possible [26, 45–47].

The findings of our study have direct implications on clinical practice. First of all, the assessment and comparison of the patterns of catch-up height gain in AGA and SGA groups present only small variances in the age range under consideration, except at age 10. At age 10, only 1 out of the 10 children did not register normal height in the AGA group, whilst approximately 1 in 5 children in the SGA subgroup still had short stature. In other words, the lower rate of catch-up growth in VLBW infants is slightly further reduced or delayed in SGA infants. On the other hand, it is important to emphasize that 1 in 3 children get normal height in both the AGA and the SGA groups between ages 2 and 4 years. This fact suggests that the implementation of the recommendation of the EMA and the Growth Hormone Research Society to postpone the beginning of rhGH therapy until the age of 4 years would be more applicable than implementing the recommendation of the FDA, which recommends the beginning of treatment at age 2 years.

The analysis of catch-up growth in ELBW infants merits particular attention. First, we detected that the majority of children that had not attained normal height by age 10 years in both the AGA and the SGA subgroups were infants born with ELBW. Second, there was a noticeable amount of children in the AGA subgroup that were not considered for hormone therapy when the response to growth hormone stimulation test was normal, in accordance with the current recommendations of the FDA, the EMA and the Growth Hormone Research Society. This fact fully explains the reason why children in the AGA subgroup with short stature at age 10 years (the majority of them were VLBW) remained in the same situation at age 14 and, presumably, in adulthood. Since current guidelines do not give consideration to the option of beginning growth hormone therapy in AGA infants with normal GH secretion, we should reckon if these criteria should be revised in the case of children born with VLBW and, especially, those with ELBW.

The multiple logistic regression analysis corroborated that ELBW and EPT infants were at higher risk of inadequate catch-up in height at 2, 4, and 10 years of age; additionally, they have an increased risk of short stature in adulthood. These results sustain the hypothesis of a potential benefit from GH treatment, independently of the adequacy of their birth weight and/or length for gestational age [18, 48–50].

In conclusion, the growth pattern of children born preterm has particular features. Approximately 85% and 53% of VLBW and ELBW infants, respectively, will attain normal height by 4 years of age. In contrast, those individuals with short stature at age 4 years are not likely to attain normal height in childhood. Catch-up in weight appears to be a decisive factor for catch-up in height, and, on this basis, we recommend a rigorous nutritional follow-up in these individuals. If these measures do not help improve catch-up in height, they may be eligible for the establishment of rhGH therapy.

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