Comparison of Postdischarge Growth in Adequate for Gestational Age and Small for Gestational Age Very Low Birthweight Infants

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Introduction: Some small for gestational age (SGA) neonates have a higher weight gain rate than adequate for gestational age (AGA) neonates. The objectives of this study were to evaluate the postdischarge growth of a cohort of very low birthweight infants to determine the percentage of those born SGA that achieve catch-up growth and whether AGA infants maintain adequate growth.

Methods: We performed a record review at the high-risk follow-up clinics of a previously paired group of infants. The infant's weight, height, and head circumference percentile at their last clinic visit were determined by using sex-adjusted curves. We also documented if the patient had presented any type of delay.

Results: Of 216 infants that were included in the original cohort, only 116 had evidence of enrollment in the clinic. The percentage of SGA that achieved catch-up growth was 18.6% ($n=59$). The percentage of adequate for gestational age that maintained adequate growth was 42.1% ($n=57$). The rate of developmental delay was not different between the groups (44.0% vs 38.6%, $P=.5$).

Conclusions: We conclude that a high percentage of high-risk infants are developing postdischarge growth delay. This study demonstrates that both SGA infants as well as AGA infants present growth problems after discharge from the hospital, which emphasizes the importance of long-term followup. (*Ethn Dis*. 2008;18[Suppl 2]:S2-118–S2-122)

Key Words: Very Low Birthweight, Weight Gain, Small for Gestational Age, Developmental Delay, Catch-Up Growth

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Introduction

Small for gestational age (SGA) infants have a higher risk of developing metabolic syndrome in adulthood, and the adequacy of early nutritional interventions is being questioned.[1–4] The prevalence of metabolic syndrome is high among Puerto Ricans and other Hispanic populations,[5] and SGA infants have an innate predisposition to chronic illness in adulthood that might be even higher in those of Hispanic origin because of the association of catch-up growth among SGA infants with insulin insensitivity.[6] Insulin insensitivity is associated with the development of type 2 diabetes. However, current nutritional guidelines continue to recommend the use of hypercaloric diets for SGA infants to promote catch-up growth.[7–12]

Catch-up growth is defined as the initial accelerated rate of growth in intrauterine growth-restricted fetuses that allows them to achieve a weight and length percentile within normal limits. This accelerated growth pattern is most commonly observed during the first year of life. Most infants that were born SGA with the capacity to achieve catch up growth will have done so by 24 months of age, but the benefits of early nutritional interventions seem to lose their effectiveness around 18 months of age.[13] Current management guidelines for infants who were born SGA include providing the option of long-term growth hormone therapy.[14] Use of growth hormone in SGA infants is indicated in patients who have not achieved catch-up growth by the age of two years.[15] In general, 10% of SGA infants do not achieve catch-up growth.

We have observed an increased rate of weight gain in a select group of Puerto Rican SGA infants while admitted in the neonatal intensive care unit (NICU), when we compared them with adequate for gestational age (AGA) infants of the same ethnic origin.[16] On the basis of our initial observations, we expected that the increased rate of weight gain seen in the NICU would continue after discharge, thus reducing the prevalence of failure to achieve catch-up growth and the need for growth hormone therapy. We also identified the need to evaluate the adequacy of the postdischarge growth rate of AGA infants. The evaluation of early growth in this population that received hypercaloric nutrition early in life is needed in light of recent findings that demonstrate an effect of nutritional programming that may increase the risk of disease later in life.[4] The primary objectives of this study were to determine the percentage of patients that achieved catch-up growth in the SGA group and ascertain the percentage of postdischarge growth failure in AGA infants. The significance of this finding is highlighted by the association of rapid initial growth followed by growth failure with a higher incidence of insulin resistance.[17,18]

Methods

A retrospective study was performed by using data from the Vermont Oxford Network forms and record review from the high-risk clinics. The Vermont Oxford Network is a network of NICUs around the world that has the goal of improving the quality of medical care for newborns. The network maintains a database for infants admitted to those NICUs.[19] In the original cohort, patients were included if they had birth weight >1500 g, were admitted to the neonatal units of the university pediatric

hospital from 1999 to 2003, and survived to discharge, including SGA and AGA infants. SGA was defined as birth weight below the 10th percentile for gestational age according to the Lubchenko growth curves. Patients were excluded if they had gastrointestinal conditions that required prolonged periods of discontinuation of enteral feedings, such as necrotizing enterocolitis stage III. Patients were also excluded if they had history of surgery of the gastrointestinal tract, birth defects, or were transferred to another institution during the first week of life.

A nested cohort was derived from the original data by pairing all SGA infants with AGA infants by using the following criteria: sex, year of birth, and birth weight (within 100 g). Clinical record review was performed for all the infants who had been paired and participated in the high-risk clinics for followup. All infants discharged from the NICU are referred to the high-risk clinics for followup, and the first appointment is coordinated before discharge. Beneficiaries of governmental health insurance would require a second referral from their primary physician.

SGA infants were considered to have achieved catch-up growth if on their last documented evaluation they had weight and height at or above the 10th percentile. Only infants with a corrected age of ≥12 months were included in the determination of catch-up growth. AGA infants were considered to have maintained adequate growth if they presented with weight and height above the 10th percentile. Sex-adjusted growth curves were used to determine percentiles.

As a secondary measure, reports of developmental delay in any of the four domains evaluated by the Denver II Developmental test were recorded. We collected the data from the Denver II Developmental test because this instrument is more accessible to primary care providers.

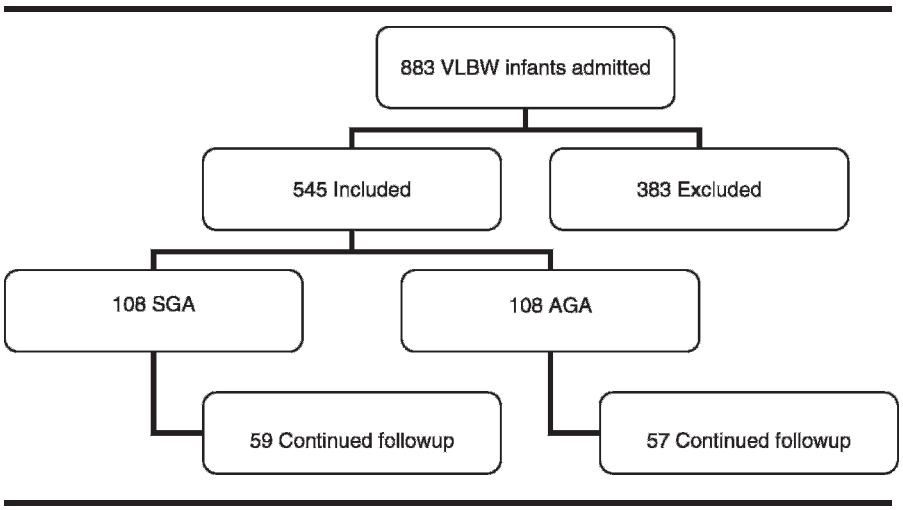

Fig 1. Distribution of small for gestational age (SGA) and adequate for gestational age (AGA) very low birthweight (VLBW) infants in neonatal intensive care units, Puerto Rico, 1999–2003.

Statistical Analysis

Nested cohort data were analyzed. Frequency distributions and percentages were used to describe the categorical variables. Means and ranges were used to describe the continuous variables. Pearson's χ^2, when appropriate, was used to determine the presence of statistical associations. Data entry and analysis were performed by using Statistix for Windows version 8.0 Epi (Analytical Software, Tallahassee, Fla). A P value$<.05$ was considered significant.

RESULTS

Of the 216 infants included in the cohort, 116 patients had evidence of any followup at the high-risk clinics, and 91 had sufficient information to evaluate for catch-up growth (SGA) or postdischarge growth failure (AGA) (Figure 1). No difference was observed in the rate of followup between SGA and AGA infants ($P=.78$). The general characteristics of the infants who had evidence of participation at the high-risk clinics are depicted in Table 1. The distribution of male patients lost to followup was higher among the AGA group ($P=.03$, Table 2). The length of stay in the NICU was statistically different among SGA and AGA infants ($P=.03$). The difference was also observed in those patients that received followup, but it did not reach significance ($P=.06$). Although the rate of comorbid conditions was statistically different between SGA and AGA infants, previously reported regression analysis revealed that SGA was the only predictive factor for the rate of weight gain that remained significant after adjusting for confounders.[20] In the group of patients that received followup, significant differences were observed in the mean percentiles for head circumference ($P=.006$), height ($P=.001$), and weight ($P<.001$) between SGA and AGA infants, showing a trend towards the lower percentiles in the SGA group (Figure 2).

When we evaluated the percentage of SGA infants that had achieved catch-up growth, we found that 82.4% of the infants had weight and height percentiles more than two standard deviations lower than the mean (10th). In the group of AGA infants, we found that 58% developed growth failure, represented by a weight and height percentile more than two standard deviations lower than the mean. When we evaluated the rate of developmental delay

Table 1. General characteristics of SGA and AGA very low birthweight infants in high-risk clinics, Puerto Rico, 1999–2003

Characteristic	SGA *n*=59	AGA *n*=57	*P* value
Male sex, % (*n*)	59.3% (35)	43.8% (25)	.1
Mean gestational age at birth, weeks (±SD)	30.5 (±2.6)	29.8 (±2.6)	.13
Mean birth weight, g (±SD)	1073 (±218)	1084 (±202)	.77
Mean discharge weight, g (±SD)	1817 (±198)	1900 (±359)	.12
Mean length of stay in NICU, days (±SD)	49.7 (±29)	60.5 (±33.5)	.06
Mean corrected age at last evaluation, months (range)	12 (4–29)	11.3 (9–30)	.6
Mean number of visits to clinic (range)	2.2 (1–6)	2.2 (1–6)	.7
Co-morbidities, % (*n*)			
Bronchopulmonary dysplasia	16.9% (10)	40.4% (23)	.005
Intraventricular hemorrhage	31.5% (18/57)	40.0% (22/55)	.4
Sepsis	20.3% (12)	38.6% (22)	.03

SGA = small for gestational age, AGA = adequate for gestational age, SD = standard deviation, NICU = neonatal intensive care unit.

reported, we did not find a significant difference between all SGA and AGA infants that had any evidence of followup (Figure 3).

DISCUSSION

Very low birthweight infants require close postdischarge followup because of risks associated with developmental delay.[21] Another element that demands special attention is the growth pattern of the infant. Close evaluation of the infant's growth curve allows for the modification of the nutritional plan both to improve growth as well as to eliminate excessive calorie supplementation. Longitudinal studies have demonstrated the effects of nutritional interventions on neonatal programming, which suggests that making these modifications early could provide a strategy for primary prevention.[3,4,22] The transition of the nutritional demands of very low birthweight infants into the community is sometimes hindered by the availability of specialized premature formulas and the economic burden that their use imposes on the family. Failure to provide adequate followup during this transition will negate the opportunity for early intervention during the critical windows of growth and development.

Based on the data from this study, only a small percentage of SGA infants achieved catch-up growth, in spite of increased rate of weight gain in the early neonatal period. This finding, along with the fact that a considerable percentage of the AGA infants developed growth failure after discharge from the hospital, highlight the importance of close growth monitoring of the very low birth weight infant. We found a statistically and clinically significant difference in the growth percentiles between SGA and AGA infants at ≈1 year of age, but the effects that this will have both in childhood and adulthood remain to be determined.

A limitation of this study is the fact that more than 50% of the patients were lost to followup at our clinics. The rate of clinic recruitment may be secondary to the gate-keeping structure of the healthcare system in Puerto Rico. Growth and development followup could also be performed at other centers, like early intervention programs, as well as by the primary care provider, which would have caused our recruitment rate to decline. The use of alternative services is supported by the finding that AGA infants lost to

Table 2. Characteristics of SGA and AGA very low birthweight infants lost to followup, Puerto Rico, 1999–2003

Characteristic	SGA *n*=49	*P* value*	AGA *n*=51	*P* value*
Male sex, % (*n*)	42.8% (21)	.09	64.7% (33)	.03
Mean gestational age at birth, weeks (±SD)	30.5 (±2.9)		29.5 (±2.5)	
Mean birth weight, g (±SD)	1144.9 (±244.9)		1125 (±225.3)	
Mean rate of weight gain, g/day (±SD)	15.99 (±4.49)		13.69 (±7.62)	
Mean discharge weight, g (±SD)	1750 (±235.7)		1829 (±378)	
Mean length of stay in NICU, days (±SD)	40.4 (±20.3)		58.1 (±36.7)	
Co-morbidities, % (*n*)				
Bronchopulmonary dysplasia	22.4% (11)	.5	45.1% (23)	.6
Intraventricular hemorrhage	27.3% (12/44)	.6	66% (33/50)	.01
Sepsis	22.4% (11)	.8	43.1% (22)	.6

SGA = small for gestational age, AGA = adequate for gestational age, SD = standard deviation, NICU = neonatal intensive care unit.
* *P* values represent the analysis of variance between those lost to followup and participants who completed followup.

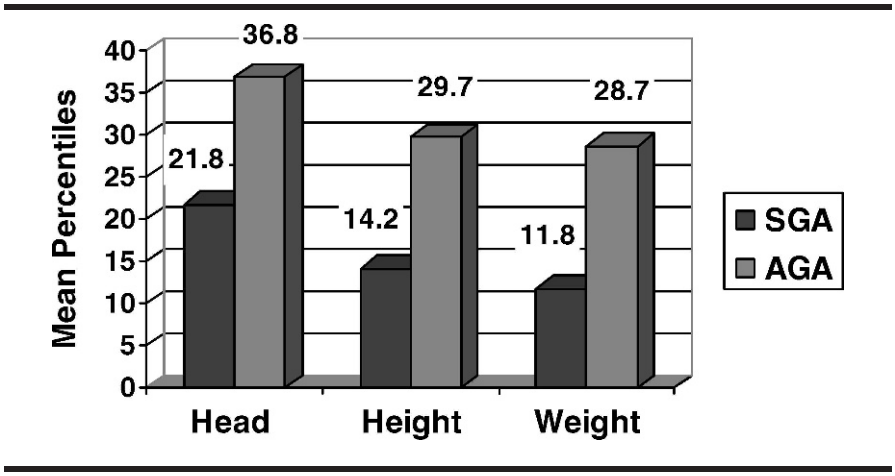

Fig 2. Mean percentiles documented at the last visit to the high-risk clinic of small for gestational age (SGA) and adequate for gestational age (AGA) very low birthweight infants, Puerto Rico, 1999–2003 (all differences significant at $P<.05$).

followup had a significantly higher rate of intraventricular hemorrhage. There are specialized follow up clinics for this condition within the early intervention program, especially if the patient suffers from posthemorrhagic hydrocephalus. There is also a possibility of bias of participation, since parents and primary physicians might have been more prone to refer to our service the care of complicated premature infants rather than premature infants who were doing well. The possibility of this bias is reinforced by the fact that no statistically significant difference was seen in the rate of delay between AGA and SGA infants. This finding contradicts the commonly held belief that SGA infants have a higher risk of developmental delay. We recognize that the Denver Developmental Test is not very sensitive or specific for the developmental evaluation for research purposes, but it represents what most primary care physicians would have available as a screening tool.

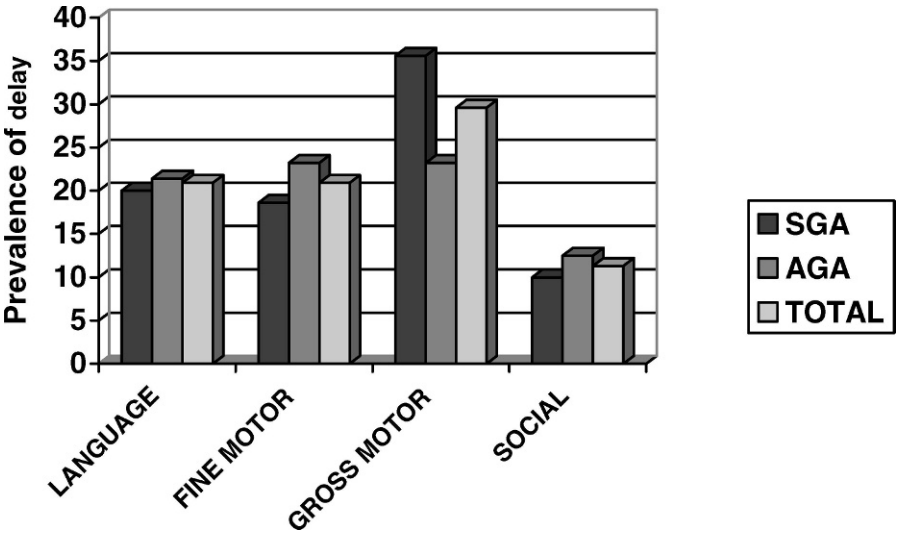

Fig 3. Prevalence of developmental delay in the dimensions evaluated by the Denver II Developmental Examination in small for gestational age (SGA) and adequate for gestational age (AGA) very low birthweight infants seen at high-risk clinics, Puerto Rico, 1999–2003 (none of the differences were significant at $P<.05$).

In the future we plan to complete follow up of the cohort to 24 months of age to confirm the finding of growth failure and the potential impact on health care based on the recommendations of long-term growth hormone therapy. Future contact with the infants will allow us to evaluate their current sociodemographic characteristics to determine the role of proposed contributing factors for growth delay, such as low socioeconomic status, crowding, level of maternal education, social deprivation, among others.

The most recent literature has proposed that patients who were born SGA present a period of early rapid growth that can later lead to chronic disease. In this study we initially identified a faster rate of weight gain of SGA infants when compared to AGA infants during the early neonatal period. We expected that this would lead to a rate of catch-up growth at least comparable to what has been reported in the literature with regard to other populations. This study demonstrates that both SGA infants as well as AGA infants present growth problems after discharge from the hospital. This finding could be secondary to many elements, including failure to adjust dietary plan as needed, lack of patient response to nutritional intervention, or characteristics of our population due to our ethnic origin. Although we cannot elucidate the cause of the discrepancy, we conclude that the findings of this study clearly demonstrate the importance of close followup of both growth and development for the high-risk infant. Changes in healthcare policy should be undertaken to guarantee that these infants will have access to the specialized health care they require.

ACKNOWLEDGMENTS

We are grateful for the assistance provided by Graciela Rabrí MS IV during the data

collection phase. This study was made possible in part by Grant Number R25 RR17589 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH).

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