EVALUATION OF PERSISTENT SHORT STATURE IN CHILDREN BORN SMALL FOR GESTATIONAL AGE WITHOUT CATCH-UP GROWTH

Ayşe Pınar Öztürk[1], Esin Karakılıç Özturan[1], Şükran Poyrazoğlu[1], Firdevs Baş[1], Feyza Darendeliler[1]

1. Istanbul University, Istanbul Medicine Faculty, Department of Pediatrics, Pediatric Endocrinology Unit, Istanbul, Turkey

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INTRODUCTION

- The majority of children born small for gestational age (SGA) demonstrate spontaneous catch-up growth in height by the age of two years.
- Approximately 10-15% of SGA newborns are at risk of having subnormal growth and persistent short stature.
- Children born SGA may have classical growth hormone (GH) deficiency or varying levels of resistance in the GH-insulin-like growth factor I (IGF-I) axis.

AIM

- The objective of the current study is to present the clinical, anthropometric, and laboratory characteristics of the 86 children (39F/49M) with persistent short stature who were born SGA.
- We aim to investigate the response of GH therapy in patients with GH deficiency, sufficiency, and insensitivity based on GH provocation tests.

METHOD

- The study population consisted of 86 short children born SGA without CUG who were followed up at the Pediatric Endocrinology Department of Istanbul University Faculty of Medicine.
- Demographic features, data on birth status (gestational age, birth weight, and length), auxological parameters, clinical features, growth/pubertal characteristics, and laboratory findings were retrieved from medical files of patients retrospectively.

RESULTS

- 29.8% of the patients were SGA just for weight, 8.8% were just for length, and 61.4% were for both.
- The rate of consanguineous marriage was 39.3%.
- 32.5% of patients had at least one parent with height-SDS ≤-2, and 10.4% had both parents with short stature.
- The frequency of premature births was 20.2%.
- Median height-SDS was -3.2.
- Besides marked short stature, a vast amount of the patients had significant clinical features. The most recurrent features associated with short stature were facial dysmorphism (55.1%) and microcephaly (55.1%).
- 41 patients (17F/41M) who reached pubertal onset, the median age at pubertal onset was 10.1 years in girls and 11.5 years in boys.
- Precocious puberty and early puberty were 6.7% and 14.6%, respectively.
- Sixty-four children were started on recombinant growth hormone(GH) treatment, and the majority (76.5%) of them were diagnosed with GH-deficiency.
- The median GH dose was 35 µg/kg/day, and duration of therapy was 3.6 years.
- Height-SDS increased significantly over the first and second years of treatment in the GH-deficient group.
- GH response in GH-deficient group was significantly greater than the non-GH deficient group in the first two years of treatment.
- Median adult-height gain SDS was 0,4 in GH-deficient patients, and it was -0,6 in the non-GH deficient group.

Table-1 Clinical characteristics of patients born small for gestational age without CUG

Background	n=86
Gender (F/M), n	37F/49M
Consanguinity, n (%)	35 (40.6%)
Gestational age (week)	40 (24-42)
Premature, n (%)	14 (16.2%)
Birth-weight SDS	-3.1 [(-4.1) - (-2.1)]
Birth length-SDS	-2.4 [(-5.2) - (-1.6)]
Maternal height-SDS ≤ 2 SDS, n (%)	-0.75 [(-1.9) - (0.54)], 28 (31.5%)
Paternal height-SDS ≤ 2 SDS, n (%)	-0.19 [(-2.21) - (0.29)], 18 (20.2%)
Both parents' height ≤ 2 SDS, n (%)	9 (10.1%)
Mid-parental height SDS	-1.45 [(-3.8) – (0,58)]
Significant clinical features	
Facial dysmorphism	49 (55.1%)
Developmental delay/intellectual disability	22 (24.7%)
Microcephaly	49 (55.1%)
Skeletal abnormalities/disproportionate stature	30 (33.7%)
Heart/renal abnormality	9 (10.1%)
Cryptorchidism (n=50)	6 (12%)
Hearing loss	2 (2.2%)

Table-2 Anthropometric characteristics at referral and puberty

At referral	
Age (years)	5.7 (0.23-16.4)
Head circumference SDS	-2.1 [(-7.8) – (0,5)]
Height SDS	-3.3 [(-8.7) – (-1.3)]
BMI SDS	-1.3 [(-6.7) – (2.3)]
Prepubertal/pubertal, n (%)	73/13 (84.9%-15.1%)
At Puberty	23F/30M
Age at onset of puberty (years)	
Female	10.1 (0.8-14.1)
Male	11.5 (5.1-14.4)
Height (cm)	
Female	125.1 (123.4-128.4)
Male	128.8 (101.1-141.1)
Height SDS	-2.7 [(-4.1) – (-1.89)]
Precocious puberty, n (%)	10, (18.8%) (4F, 6M)
Early puberty, n (%)	13 (24.5%) (8F,5M)
Delayed puberty (n,%)	4 (7.5%) (2 F, 2M)

Table-3. Anthropometric characteristics of patients at recent evaluation

	with rhGH	without rhGH	Intergroup comparison
Total group			
Overall (n=)	64	23	
Age (years)	13.3 (6.1-19.5)	11.6 (5.9-19)	0.03
Head circumference SDS	-2.1 [(-5.9) – (1.4)]	-3 [(-5.7) – (-0.4)]	0.2
Height SDS	-3 [(-6.9) – (-0.8)]	-2.9 [(-4.7) – (-1.7)]	0.9
BMI SDS	-1.2 (-4.2 - 3.4)	-1.7 (-4.4-1.9)	0.2
Sitting height/height SDS	-0.3 [(-3.2) – (5.3)]	-0.3 [(-2.5) – (1.6)]	0.2
Patients who achieved the final height			
Overall (n=)	13	6	
Age (years)	17 (12.9-19.5)	17 (16.3-19)	p=0.7
Head circumference SDS	-2.5 [(-5.6) – (-1.7)]	-2.5 [(-3.4) – (-1.5)]	p=0.9
Height SDS	-3 [(-4.9) – (-1.2)]	-3.7 [(-4.5) – (-2.1)]	p=0.4
BMI SDS	-0.8 (-4.2-1.1)	-2.5 (-4.3-1.9)	p=0.3
Sitting height/height SDS	-0.1 [(-2.4) – (0.6)]	-0.8 [(-2.5) – (1.6)]	p=0.8
FAH SD-MPH SDS	-1.5 [(-3.5) – (-0.7)]	-1.3 [(-3.9) – (-0.1)]	p=0.8

F; female, M; Male, SDS; Standard deviation score, BMI; Body mass index, FAH; Final adult height, MPH; Midparental height, SDS; Standard deviation score, rhGH; Recombinant human growth hormone
Median and minimum-maximum range or % values are given

CONCLUSIONS

- Short-statured patients born SGA should be examined in terms of accompanying features.
- Although the response to GH treatment is a better GH-deficient group, final adult-height may remain below the general population.
- Further studies are needed to elucidate the etiology in SGA with persistent short stature.

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CONTACT INFORMATION

Adress: Istanbul University, Istanbul Faculty of Medicine, Department of Pediatrics, Pediatric Endocrinology Unit, 34104, Fatih/İSTANBUL

E-mail: pozturk@hotmail.com