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Effects of Gender and Gestational Age on Height Outcomes in Very Young Children Born Small for Gestational Age treated with Growth Hormone.

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Background

Short children born small for gestational age (SGA) with poor growth during the first years of life often have persistent short stature during childhood and as adults. Growth hormone (GH) therapy has been shown to be effective in improving height in these children. GH treatment was approved by the US Food and Drug Administration (FDA) for SGA children who fail to manifest catch-up growth by the age of 2 years and by the European Agency for the Evaluation of Medicinal Products for SGA children older than 4 years of age.

Aim

To evaluate the effects of gender and gestational age (GA) on outcomes of growth hormone (GH) treatment in very young children born SGA.

Patients and Methods

We identified subjects enrolled in KIGS (Pfizer International Growth Database) who met the following criteria: SGA patients on GH treatment with birth length and/or weight below -2 SDS, with age at start of therapy older than 2 and less than 4 years and between 4 and 6 years. Subjects with a GA of ≤ 37 weeks are grouped as Preterm and GA > 37 weeks are grouped as Term. In total, 620 SGA children on GH treatment were followed longitudinally for 3 years.

For comparison between patient groups, Wilcoxon test was used. SAS® version 9 for Sun Solarix (SAS Institute, Cary, North Carolina) was used for all statistical analyses. SDS = standard deviation score;
* p<0.01

Results

Study Groups (Table 1)

- **2-4 years age:** n=156 (100 boys); median age 3.3 years; 50% with GA ≤ 37 weeks
- **4-6 years age:** n=464 (284 boys); median age 4.9 years; 42.2% with GA ≤ 37 weeks

Table 1 Clinical characteristics before and during GH treatment

	SGA 2-4 years			SGA 4-6 years			
	N	Median	10°/90° centiles	N	Median	10°/90° centiles	
Baseline							
Gestational age, wks	156	37.5	31/40	464	38	31/40	
Birth weight SDS	156	-2.5	-3.9/-1.5	464	-2.4	-3.7/-1.4	
Birth length SDS	133	-2.7	-4.8/-1.4	425	-2.6	-4.1/-1.6	
Age, years	156	3.3	2.6/3.9	464	4.9	4.2/5.8	*
Height SDS (Prader)	156	-3.9	-5.4/-2.9	464	-3.4	-4.5/-2.6	*
1st yr on GH							
Height SDS (Prader)	156	-3.0	-4.8/-1.9	464	-2.6	-3.8/-1.7	*
Delta Height, SDS	156	0.9	0.4/1.5	464	0.8	0.4/1.3	*
Height velocity, SDS	156	2.0	0.1/4.3	464	3.1	0.8/5.6	*
3rd yr on GH							
Height SDS (Prader)	156	-2.2	-3.8/-1.1	464	-2.0	-3.1/-0.9	*

Study Groups by Preterm/Term (Table 2)

- **Preterm:** Preterm children in the 4-6 yrs group were younger than the term ones at GH start (4.8 vs 5.0 yrs, p<0.01), leaner weight SDS (-3.4 vs -2.9, p<0.001) and had a lower adjusted parental height (-2.4 vs -2.1, p< 0.01)
- **Term:** In the 2-4 yrs group, compared to term ones, preterm children received higher GH dose (0.38 vs 0.32 mg/kg/wk, p<0.05) and presented higher HV SDS only during the first year of therapy (2.5 vs 1.7, p<0.05)

Results, cont

Table 2 Clinical characteristics of term and preterm SGA children

	Preterm 2-4 years (N=78)		Term 2-4 years (N=78)			Preterm 4-6 years (N=196)		Term 4-6 years (N=268)		
	Median	10°/90° Centiles	Median	10°/90° Centiles		Median	10°/90° Centiles	Median	10°/90° Centiles	
Baseline										
Gestational age, wks	34	28/37	39	38/41	*	34	28/37	40	38/41	*
Birth weight SDS	-2.4	-3.7/-1.5	-2.7	-4.1/-1.5		-2.5	-3.5/-1.4	-2.4	-3.8/-1.4	
Birth length SDS	-2.7	-4.6/-1.4	-2.7	-5.1/-1.3		-2.7	-4.2/-1.7	-2.5	-3.9/-1.3	
Age, years	3.4	2.5/3.8	3.2	2.6/3.9		4.8	4.1/5.7	5.0	4.2/5.8	*
Height SDS	-3.9	-5.2/-2.8	-3.9	-5.9/-3.0		-3.4	-4.6/-2.5	-3.5	-4.5/-2.6	
GH dose mg/kg/wk	0.38	0.21/0.47	0.32	0.18/0.43	*	0.25	0.19/0.42	0.25	0.18/0.41	
1st yr on GH										
Weight SDS	-3.3	-4.9/-1.8	-2.8	-5.3/-1.3		-2.6	-4.0/-1.1	-2.1	-3.7/-1.0	*
Ht-MPH SDS	-1.9	-3.8/-0.9	-1.5	-5.1/-0.3		-1.6	-3.3/-0.6	-1.3	-3.2/0.0	*
Height Velocity, SDS	2.5	0.4/4.7	1.7	-0.5/4.0	*	3.1	0.9/5.6	3.3	0.8/5.6	

Study Groups by Gender

- **2-4 years age:** girls presented lower height SDS (HSDS) at start of treatment (-4.2 *vs* -3.8; p<0.01), an higher increase in height compared to boys, during the first year Delta HSDS (1.0 vs 0.9; p<0.05), with disappearance of the difference in height at 3 years of treatment (Table 3, Figure 1a).
- **4-6 years age:** girls were also shorter HSDS (-3.6 vs -3.3; p<0.01), but their height velocity (HV) during the first year of treatment was lower (2.7 *vs* 3.4 SDS; p<0.01); Height SDS was still different at 3 years of therapy (-2.2 *vs* -1.9 SDS; p<0.05) (Table 3, Figure 1b).

Table 3 Clinical characteristics of girls and boys born SGA

	2-4 years (Females N=56)		2-4 years (Males N=100)			4-6 years (Females N=180)		4-6 years (Males N=284)		
	Median	10°/90° centiles	Median	10°/90° centiles		Median	10°/90° centiles	Median	10°/90° centiles	
Baseline										
Gestational age, wks	38	32/41	37	31/40		38	32/40	38	31/40	
Birth weight SDS	-2.4	-3.9/-1.1	-2.6	-4.0/-1.5		-2.4	-3.6/-1.4	-2.4	-3.8/-1.4	
Birth length SDS	-2.4	-5.1/-0.7	-3.0	-4.8/-2.0	*	-2.6	-3.9/-1.5	-2.6	-4.4/-1.6	
Age, years	3.4	2.8/3.9	3.3	2.6/3.8		4.8	4.1/5.7	5.0	4.2/5.9	
Height SDS	-4.2	-6.0/-3.2	-3.8	-5.0/-2.8	*	-3.6	-4.8/-2.6	-3.3	-4.3/-2.5	*
GH dose mg/kg/wk	0.32	0.18/0.45	0.37	0.21/0.45		0.26	0.19/0.41	0.25	0.18/0.42	
1st yr on GH										
Ht-MPH SDS	-1.9	-4.9/-1.0	-1.8	-4.1/-0.2		-1.4	-3.2/-0.0	-1.4	-3.2/-0.0	
Height Velocity, SDS	2.1	-0.4/4.3	2.0	0.2/4.4		2.7	0.6/5.6	3.4	1.1/5.6	*
Delta height SDS	1.0	0.4/1.8	0.9	0.4/1.4	*	0.8	0.4/1.4	0.8	0.4/1.2	
3rd yr on GH										
Height SDS (Prader)	-2.5	-4.0/-1.0	-2.1	-3.8/-1.1		-2.2	-3.6/-0.9	-1.9	-3.1/-0.9	*

Figure 1a:
SGA 2-4 years. Female (F) vs. Male (M) comparing Height SDS at GH start (0), first year (1) and 3 years on GH (3)

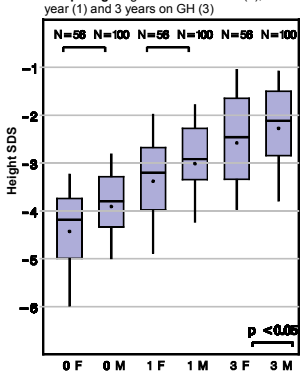
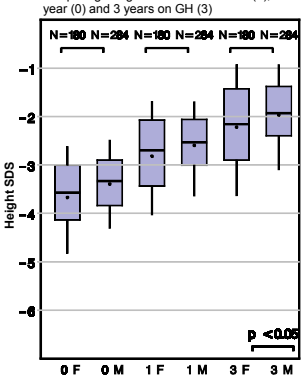


Figure 1b:
SGA 4-6 years. Female (F) vs. Male (M) comparing Height SDS at GH start (0), first year (0) and 3 years on GH (3)



Conclusion

Among very young SGA children, girls and those born preterm were reported to be shorter at start of GH treatment. All presented a significant improvement in height during GH therapy.

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