Response to Growth Hormone treatment in the very young with Growth Hormone deficiency

S Çetinkaya[1], Ş Poyrazoğlu[2], Yeşilkaya E[3], Z Aycan[1,4], Z Şıklar[5], M Berberoğlu[5], Z Atay[6], A Bereket[6], O Ercan[7], E Mengen[8], F Demirel[4,9], Ş Darcan[10], F Darendeliler[2]

[1]Dr Sami Ulus Obstetrics and Gynecology, Children's Health and Disease Training and Research Hospital, Clinics of pediatric endocrinology, Ankara, Turkey
[2]Pediatric Endocrinology Unit, Istanbul Faculty of Medicine, and Institute of Child Health, Istanbul University, Istanbul, Turkey
[3] Gülhane Military Medicine Academy, Department of Pediatric Endocrinology, Ankara, Turkey
[4]Yıldırım Beyazıt University Faculty of Medicine, Ankara, Turkey
[5]Ankara University School of Medicine, Department of Pediatric Endocrinology, Ankara, Turkey
[6]Department of Pediatric Endocrinology, Marmara University, Pendik, Istanbul, Turkey
[7]Pediatric Endocrinology and Adolescent Divisions, Pediatrics Department, Cerrahpasa Medical Faculty, Istanbul University , Istanbul , Turkey
[8]Division of Pediatric Endocrinology, Faculty of Medicine, Cukurova University, Adana, Turkey
[9]Department of Endocrinology, Ankara Children's Hematology and Oncology Training Hospital, Turkey
[10]Department of Pediatric Endocrinology, Ege University School of Medicine, Izmir, Turkey.

AIM

Data on response to growth hormone (GH) treatment in the very young children with GH deficinecy is scarce. The aim of this study was to evaluate the growth response in such children in a national multicentre study and to analyze the factors affecting the growth response.

MATERIALS and METHODS

In this study, we retrospectively evaluated the files of GH deficiency patients who had started GH treatment between 0-3 years of age who were being followed in 14 different centers from different regions of Turkey between 19 February 2014 and 23 October 2014. The study was approved by the Clinical Studies Ethics Committee.

All collected data were obtained from patient hospital records. An electronic case recording form (CRF) was created. The CRF covered demographic features, as well as clinical and laboratory findings of the patients. The CRF was uploaded to the website of FAVOR Web Registry System (www.favorsci.org). Data entered in the registry were checked for consistency by one of the authors (SÇ). The time given for patient enrollment was eight months. By the end of the deadline the collected patient record data were entered to Microsoft Excel database and subsequently transferred to SPSS for Windows statistical software for statistical analysis.

The duration of GH treatment was accepted to be at least 12 mo. The patients were further subdivided according to isolated vs multiple pituitary hormone deficiency (MPHD) and age at onset of therapy: 0-12 mo vs 12-36 mo. Patients with MPHD received appropriate replacement therapy. Mean±SD and range values are given in the Tables.

RESULTS

There were 42 patients with GH deficincy (23M, 19F) with a peak GH response (after GH stimulation test or at hypoglycemia) of 0.69±0.14 ng/ml. 30 had MPHD and 12 had isolated GH deficiency. The mean age at onset of GH therapy was 11.2±1.03 mo. Mean GH dose used was 31.7±1.4μg/kg/day. Results of GH therapy over one year are shown in Table 1.

Table 1: Background data and results of GH therapy over one year in all patients with GH deficiency

Background data		
Gestational age (week)	39.0±0.3 / 32.0-42.0	
Birth weight (kg)	3.1±0.8 / 1.8-4.1	
Birth length (cm)	48.0±0.6 / 42.0-52.0	
GH peak (ng/ml)	0.69±0.14 / 0.005-4.4	
GH dose (μg/kg/d)	31.7±1.4 / 20-70	
GH therapy results	At Onset	At 1 yr of therapy
Age (month)	11.2±1.0 / 1-25	23.2±6.7 / 13-37
Length (cm)	61.8±1.2 / 47-77.5	77.4±1.0 / 64-92.5
Length SDS	-4.0±1.4 / -7.0 to -0.7	-2.0±2 / -6.0 to 1.4
Weight (kg)	6.3±0.3 / 3-12	9.7±0.4 / 5.5-16.1
Weight SDS	-3.5±1.6 / -7.2 to 0.1	-2.0±2.4 / -5.9 to -1.9
BMI (kg/m²)	15.8±0.3 / 11.9-21.1	16.0±0.3 / 13.0-23.7
BMI SDS	-0.7±1.5 / -3.9- to -2.3	-0.3±1.7 / -2.9 to -3.7
Δ Length	15.4±0.7 / 8-24	
Δ Length SDS	1.7±0.2 / -0.7 to 3.7	
Δ Body weight	3.5±0.3 / 1.2-9.4	
Δ Body weight SDS	1.5±0.2 / -1.5 to 4.0	

In MPHD Group 1st year response was significantly higher (16.5±4.2cm) than in the isolated GH deficiency group (12.8±3.3cm) (p=0.014) (Table 2).

Table 2: Comparing 1st year growth response between the MPHD and isolated GH Deficiency Group

Background data				
Gestational age (week)	39.1±1.9 / 32-42		38.9±1.7 / 35-41	
Birth weight (kg)	3.1±0.5 / 1.8-4.1		3.0±0.4 / 2.2-3.8	
Birth length (cm)	48.5±1.8 / 46-52		46±3.6 / 42-49	
GH peak (ng/ml)	0.6±0.9 / 0.05-4.4		0.08±0.03 / 0.06-0.1	
GH dose (μg/kg/d)	30±6.0 / 20-45		35.6±13.0 / 20-70	
GH therapy results	MPHD n=30		Isolated GH Deficiency n=12	
	At Onset	At 1 yr	At onset	At 1 yr
Age (month)	9.4±6.7 / 1-25	21.4±6.7 / 13-37	16±4.1 / 10-23	28±4.1 / 22-35
Length (cm)	59.9±7.6 / 47-77.5	76.4±6.6 / 64-92.5	66.8±4.9 / 59-76	79.6±5.8 / 72.5-88
Length SDS	-3.9±1.5 / -7.0 to -0.7	-2.2±1.6 / -6 to 1.4	-4±1.09 / -6.04 to -2.5	-2.4±1.2 / -4.8 to -0.2
Weight (kg)	5.8±2.2 / 3-12	9.2±2 / 5.5-13.6	7.4±1.5 / 5.2-9.9	10.9±2.8 / 7.9-16.1
Weight SDS	-3.3±1.6 / -7.2 to 0.06	-2.0±1.8 / -5.9 to 1.8	-3.11±1.5 / -5.9 -0.8	-1.4±1.9 / -3.31 to 1.9
BMI (kg/m²)	15.6±2.2 / 11.9-20	15.6±1.7 / 13.13-20.58	16.4±2.2 / 13.59-21.1	17.1±3.1 / 13.0-23.7
BMI SDS	-0.96±1.5 / -3.9 to 2.06	-0.6±1.2 / -2.6 to 2.0	-0.34±1.4 / -2.3 to 2.3	0.46±1.8 / -2.9 to 3.7
Δ Length	16.5±4.2* / 9-24		12.8±3.2* / 8-18.5	
Δ Length sds	1.7±1.1 / -0.7 to 3.7		1.6±0.9 / 0.3 to 3.3	
Δ Body weight	3.5±1.8 / 1.2-9.4		3.6±1.4 / 1.6-6.2	
Δ Body weight sds	1.27±1.2 / -1.5 to 4.0		1.7±1.0 / -0.1 to 3.1	

* statistically significant differences

In the group started GH between 0-12 mo the response (18.0±4.2 cm) was higher than in the ones started between 12-36 mo of age (13.3±3.1 cm) (p=0.013) (Table 3).

Table 3: Comparing growth response between the group starting GH between 0-12 mo and 12-36 mo of age

Background data	0-12 mo n=20		12-36 mo n=22	
Gestational age (week)	39.2±1.54 / 37-42		38.9±2.09 / 32-42	
Birth weight (kg)	3.16±0.473 / 2.45-4.01		3.05±0.539 / 1.8-4.13	
Birthlength (cm)	48.1±1.45 / 46-50		47.8±3.4 / 42-52	
GH peak (ng/ml)	0.44±0.64 / 0.025-2.28		0.7±0.8 / 0.05-3.06	
GH dose (μg/kg/d)	33.4±10.36 / 20-70		30.4±7.12 / 20-45	
GH therapy results	At Onset	At 1 yr	At onset	At 1 yr
Age (month)	4.8±3.9* / 1-12	17.5±3.9 / 13-24	16.04±4.3* / 5-25	28±4.3 / 17-37
Length (cm)	55.7±4.4 / 47-64	73.8±5.5 / 64-81	66.9±5.7 / 56-77.5	80.2±5.8 / 72.5-92.5
Length SDS	-4±1.5 / -7.0 to-0.7	-2.2±1.9 / -6 to 1.4	-3.9±1.3 / -6.4 to -1.4	-2.3±1.1 / -4.8 to 0.1
Weight (kg)	4.8±1.2* / 3-6.9	8.8±1.9 / 5.5-13.5	7.4±2.0* / 4.2-12	10.5±2.4 / 6.9-16.1
Weight SDS	-3.3±1.2 / -5.3 to -0.5	-2.0±2.0 / -5.9 to 1.8	-3.17±1.8 / -7.2 to 0.06	-1.7±1.7 / -4.4 to 1.9
BMI (kg/m²)	15.2±2.0 / 11.9-19.8	16.0±1.8 / 13.4-20.6	16.31±2.3 / 12.3-21.1	16.1±2.6 / 13.0-23.7
BMI SDS	-1.2±1.2 / -3.3 to 1.7	-0.6±1.3 / -2.4 to 2.1	-0.4±1.6 / -3.9 to 2.3	-0.06±1.7 / -2.9 to 3.7
Δ Length	18±4.2* / 10-24*		13.3±3.1* / 8-18.5*	
Δ Length SDS	1.8±1.2 / -0.7 to 3.7		1.6±1.0 / -0.6 to 3.3	
Δ Body weight	4.1±2.0 / 1.2-9.4		3.02±1.25 / 1.3-6.2	
Δ Body weight SDS	1.3±1.4 / -1.5 to 4.0		1.5±1.0 / -0,7 to 3.1	

*statistically significant differences

There was a significant increase in length SDS (p=0.000), weight SDS (p=0.000) and BMI SDS (p=0.02) over one-year of therapy. Height velocity over one year showed positive correlation with weight increment (r=0.38), but did not show correlation with birth weight, peak GH level, GH dose and BMI (Figure 1,2,3,4).

There was no difference between girls and boys with respect to the growth response. Neither was a difference in growth response between those with minipuberty or not.

Multiple regression analysis did not reveal a significant parameter to explain the differences in growth response.
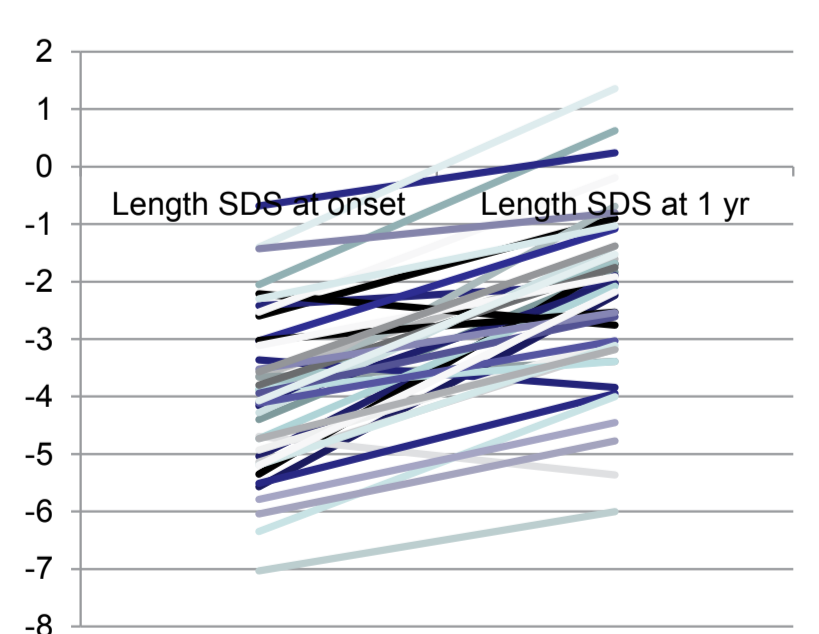

Figure 1: Changes in length SDS

Figure 2: Changes in weight SDS
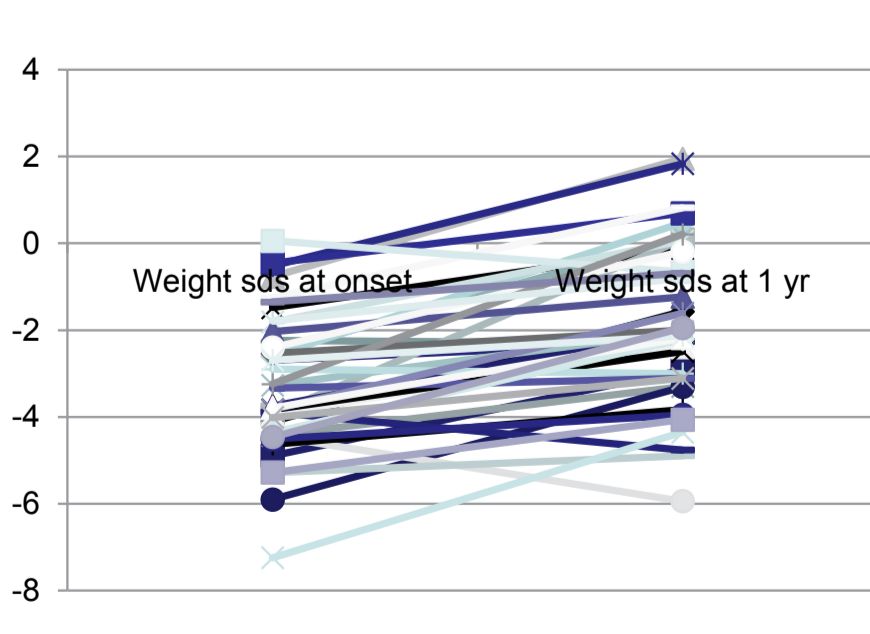
Figure 3: Changes in BMI SDS
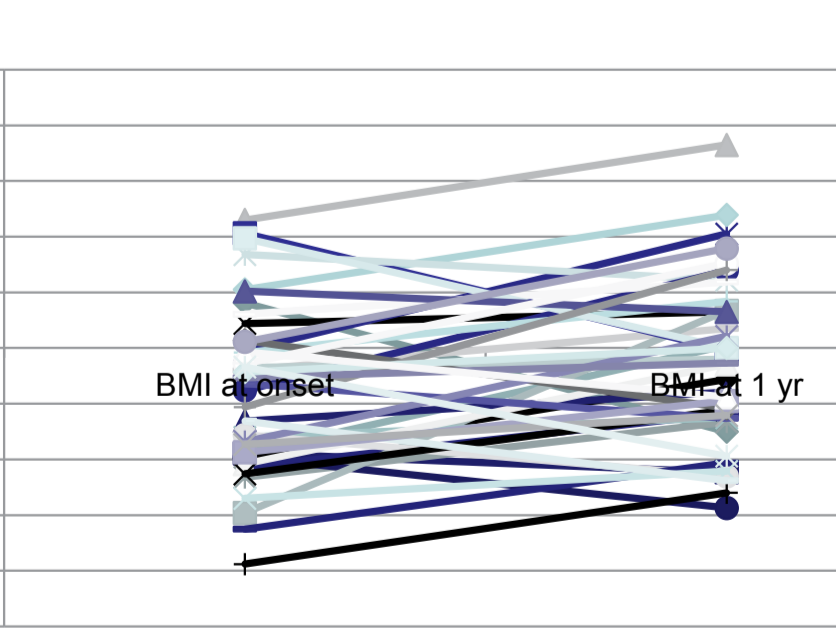
Figure 4: Correlation between weight gain and height gain
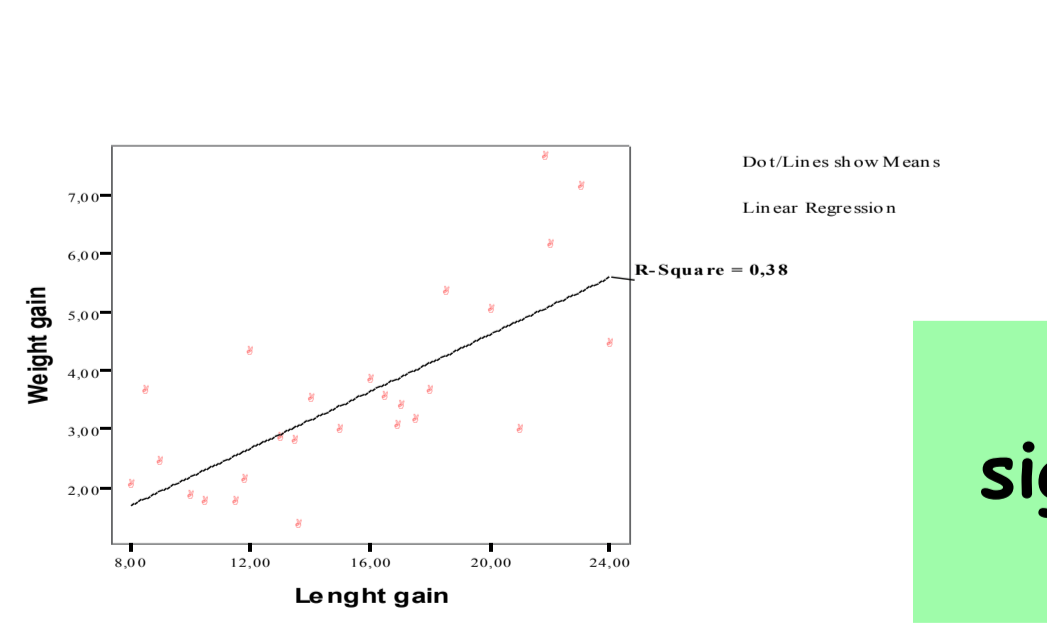
CONCLUSION

Among children with GH deficiency, young children with MPHD respond beter than isolated GH deficiency and those children aged between 0-12 mo at onset of therapy respond better than 12-36 mo children. The most significant factor in growth response was weight gain.

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