EVALUATION OF THE CLINICAL AND LABORATORY PARAMETERS AND FINAL ADULT HEIGHT IN PATIENTS TREATED WITH RECOMBINANT HUMAN GROWTH HORMONE

E Sayin[1], A Altincik[1] , B Özhan[1]

[1]Pamukkale University of Medicine, Department Pediatric Endocrinology, Denizli, Turkey

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Introduction

Growth hormone (GH) theraphy increases height prognosis, improves final height in patients with GH deficiency and in some conditions of short stature without GH deficiency. Responsiveness to GH depends on several factors. Recognizing these factors will help to optimize the long-term response to GH treatment.

Aim

The aim of this study was to investigate the clinical and laboratory features of patients who received recombinant human growth hormone (rhGH) treatment and to investigate thefactors that determine the response to rhGH treatment.

Method

The clinical features of children treated with rhGH at least one year were retrospectively analyzed. Patients were grouped according to diagnosis; isolated GH deficiency (IGHD), multiple pituitary hormone deficiency (MPHD), Turner syndrome, other syndromes, idiopathic short stature (ISS).

A peak GH concentration below 10 mg/L has been used to support GHD diagnosis. Turner syndrome diagnose was based on karyotype analysis. ISS was defined as non-GH-deficient short stature (height standard deviation score (SDS) ≤ –2.25) with other causes of short stature has been excluded.

Auxological data were expressed as standard deviation scores (SDS) calculated using Turkish national references.

In total 268 patients (156 boys, 112 girls) with mean age of 11,3 ±3,07 were included in the study. 231 (86,1%) of patients were treated with GH due to isolated GHD, 15 (5,5%) due to ISS, 6 (2,2%) patients due to MPHD, 8 (2,9%) due to Turner syndrome and 8 (2,9%) due to other syndromes.

Results

Auxological and clinical data of entire group is given in table 1.

The mean age and IGF-1 levels of patients with MPHD was lower than those of the IGHD (p =0.04 and p=0.01). The peak GH response was significantly lower in patients with MPHD than all of the other groups.

Height gain (cm/year) of IGHD group at the first year was higher than that of Turner group (p=0.04) (figure 1), however delta height SDS in first year (change in height SDS) were similar between entire group (figure2).

Height gain was highest at the first year of therapy (figure 3 & 4).

Table 1. Auxological and clinical data of entire group at the time of diagnosis.

		Age	Height	Height SDS	Weight (kg)	Weight SDS	BMI (kg/m²)	BMI SDS	CA-BA	IGF-1	IGF-1 SDS	Peak GH (ng/mL)	Somatropin dosage (mcg/kg/d)	1.year height gain (cm/year)	1.year height SDS gain
IGHD N:231	Mean	11,56	131,19	-2,65	32,63	-1,72	18,19	-0,42	2,18	176,85	-0,75	5,65	36,20	8,99	0,59
	SD	2,84	16,65	0,69	11,96	1,12	3,78	1,22	1,20	104,99	1,09	2,58	6,57	1,90	0,38
MPHD N:6	Mean	8,12	108,10	-3,45	26,12	-1,78	20,29	0,35	2,14	54,64	-2,31	1,65	34,83	7,45	0,41
	SD	4,21	24,45	1,92	18,26	3,05	9,26	1,95	0,66	34,09	1,29	2,21	5,74	0,99	0,24
Turner * Syndrome N:8	Mean	10,91	124,83	0,82	35,96	-0,82	21,74	0,93	2,06	215,27	-0,55		43	6,65	0,24
	SD	4,3	20,95	0,95	15,65	1,09	4,76	1,08	1	125,36	1,12		8,53	1,46	0,61
Other syndromes N:8	Mean	8,94	113,91	-3,3	23	-1,54	17,24	0,1	2,6	109,82	-1,65	6,25	29,25	8,08	0,76
	SD	4,33	19,92	1,01	10,09	1,95	1,62	1,06	0,91	102,35	1,25	2,98	3,84	1,89	0,55
ISS N:15	Mean	10,08	121,1	-3,1	25,52	-2,2	16,73	-0,55	2,64	123,49	-1,2	9,63	33,3	8,6	0,61
	SD	3,57	18,7	0,48	9,64	0,76	2,12	0,95	0,64	70,14	0,81	4,24	6	1,21	0,33

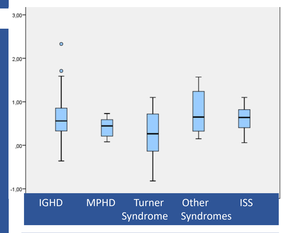

Figure 1. Height gain (cm/year) of groups at first year .

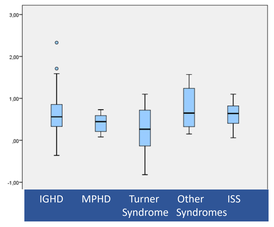

Figure 2. Delta height SDS of groups at first year .

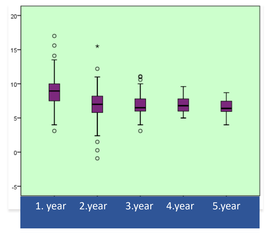

Figure 3. Height gain (cm/year) of entire group year by year.

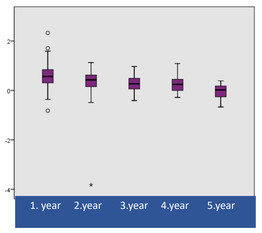

Figure 4. Delta height SDS of entire group year by year.

Table 2. **Year to year response to rhGH therapy in IGHD group.**

	First year response (n=231)			2.year response (n=133)			3.year response (n=45)			4.year response(n=23)			5.year response (n=9)		
	Time at diagnosis	1.year	p	1.year	2.year	p	2.year	3.year	p	3.year	4.year	p	4.year	5.year	P
Height(cm)	131.1±16.6	140.98±15.4	<0.01	138.41±15	145.60±14.9	<0.01	137.7±14.7	145±14.9	<0.01	138.4±14.7	145.3±14.3	<0.01	136.6±10.8	143.36±10.9	<0.01
Height SDS	-2.65±0.69	-2.06±0.65	<0.01	-2.01±0.67	-1.73±0.70	<0.01	-2.04±0.74	-1.75±0.78	<0.01	-2.0±0.83	-1.73±0.79	<0.01	-1.73±0.55	-1.71±0.64	0.9
BMI	18.19±3.78	19.17±9.76	0.11	19.39±12.4	19.04±4.46	0.74	18.07±2.69	19.07±3.3	<0.01	18.30±3.39	19.21±3.08	<0.01	17.71±2.64	18.86±2.75	0.01
BMI SDS	-0.42±1.22	-0.56±1.22	<0.01	-0.49±1.21	-0.24±2.83	0.28	-0.83±2.51	-0.34±1.2	0.18	-0.23±1.16	-0.27±1.04	0.85	-0.36±0.89	-0.24±0.78	0.50
IGF-1	177±105.7	355.1±169	<0.01	314.9±168.8	388.9±207.4	<0.01	309.28±111.6	368.9±155.3	0.01	310.9±92.7	406.4±140.2	0.01	370.2±93.4	442.8±133	0.23
IGF-1 SDS	-0.76±1.08	0.97±1.52	<0.01	1.14±1.84	1.01±1.67	0.50	1.02±1.35	1.01±1.50	0.97	1.05±1.71	0.77±1.11	0.58	1.36±0.93	1.13±1.87	0.79

A negative correlation was found between the height gain (cm/year) in the first year and peak response to GH stimulation test (p= 0.00 r=-0.27), serum IGF-1 level at diagnosis (p= 0.013, r=-0.16), IGF-1 SDS (p= 0.018, r=-0.15).

There was a positive correlation between height gain (cm/year) in the first year and target height (p=0.001, r= 0.22), weight SDS (p= 0.03 r= 0.13), BMI (p= 0.02 r= 0.15), BMI SDS (p= 0.001, r= 0.21).

A negative correlation was found between the change in height SDS in the first year (first year delta height SDS) and height SDS at the beginning of the treatment (p=<0.001, r=-0.38), peak GH response to GH stimulation test (L-Dopa) (p=0.017 r=-0,158), IGF-1 SDS (p= 0.001, r=-0.211).

Thirty five patients (21female, 14 boy). had final height data. Mean final adult height (FAH) SDS was -1,31 ±0,78 and final delta height SDS (the change in height SDS between the beginning and end of treatment) was 1,16 ±0.51. FAH SDS was -1,36±0,51 in males; -1,27±0,93 in females (p=0.59); -1,69±0,93 in the patients who were prepubertal at beginning of treatment and-1.16±0.81 in the patients who were pubertal at beginning of treatment (p=0.1). FAH SDS (-1.31 ±0.78) was similar to the target height SDS (-1.23±0.71) (p=0.64).

FAH was correlated with height SDS at the beginning of treatment(p<0.001, r=0.65), the growth rate(cm/year) in the first year (r=0.33, p=0.02).

A positive correlation was found between final delta height SDS and first year delta height SDS (r=0.40 p<0.001), growth rate (cm/year) in the first year (r=0.69, p<0.001), difference between chronological age and bone age (r=0.26, p=0.04).

There was a negative correlation between peak GH test response and final delta height SDS (r=-0.19, p=0.04).

Conclusions

- Height gain (cm/year) is best at first year of the rhGH therapy.
- Height gain in the first year of rhGH therapy is positively correlated with weight, BMI status and target height.
- Height gain in the first year of rhGH therapy is negatively correlated with peak GH response to stimulation test, IGF-1 levels.
- The predictors of FAH are; height SDS at the beginning of the therapy and the height gain (cm/year) in the first year of the therapy.
- Maximal response to rhGH therapy (final gain of height SDS) is achieved in patients with severe GH deficiency (poor GH response to stimulation test).

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