Long-term results of GH therapy in GH-deficient children treated in Albania

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Background

Recombinant human growth hormone, which was approved in 1985, made available a reliable and virtually unlimited resource to replace human pituitary growth hormone. Idiopathic growth hormone deficiency is the main indication for treatment in more than one half of children receiving growth hormone therapy. Growth hormone treatments aim to normalize growth, correct health problems associated with growth hormone deficiency, and help patients achieve an adult height in the normal range for the general population and for familial genetic potential. Long term studies had shown that it was possible to achieve the above objectives in patients who were optimally treated.

In Albania, the use of growth hormone has been increasing slowly since 2001 due to high cost of treatment, lack of funding for patients and lack of public awareness until recently.

Moreover, data regarding response to treatment and factors affecting final height in our local population has not been available.

Objective and hypotheses

To evaluate the efficiency of recombinant growth hormone (rhGH) in improving adult height in children with growth hormone deficiency (GHD).

Materials and methods

This is an observational follow up study which enrolled all Albanian children diagnosed with GHD [isolated (IGHD) or multiple pituitary hormone deficiencies (MPHD)] and treated with rhGH, who had attained final height. Patients with syndromes, tumors, other systemic diseases were excluded. Their treatment started between 2001 and 2015. Main outcome measures were: annual changes in height, change in height between the start of treatment and adulthood height and the importance of the factors that influence on final height.

Results were expressed as mean ± standard deviation (SD). Data was analyzed using the IMB SPSS Statistics Version 20.

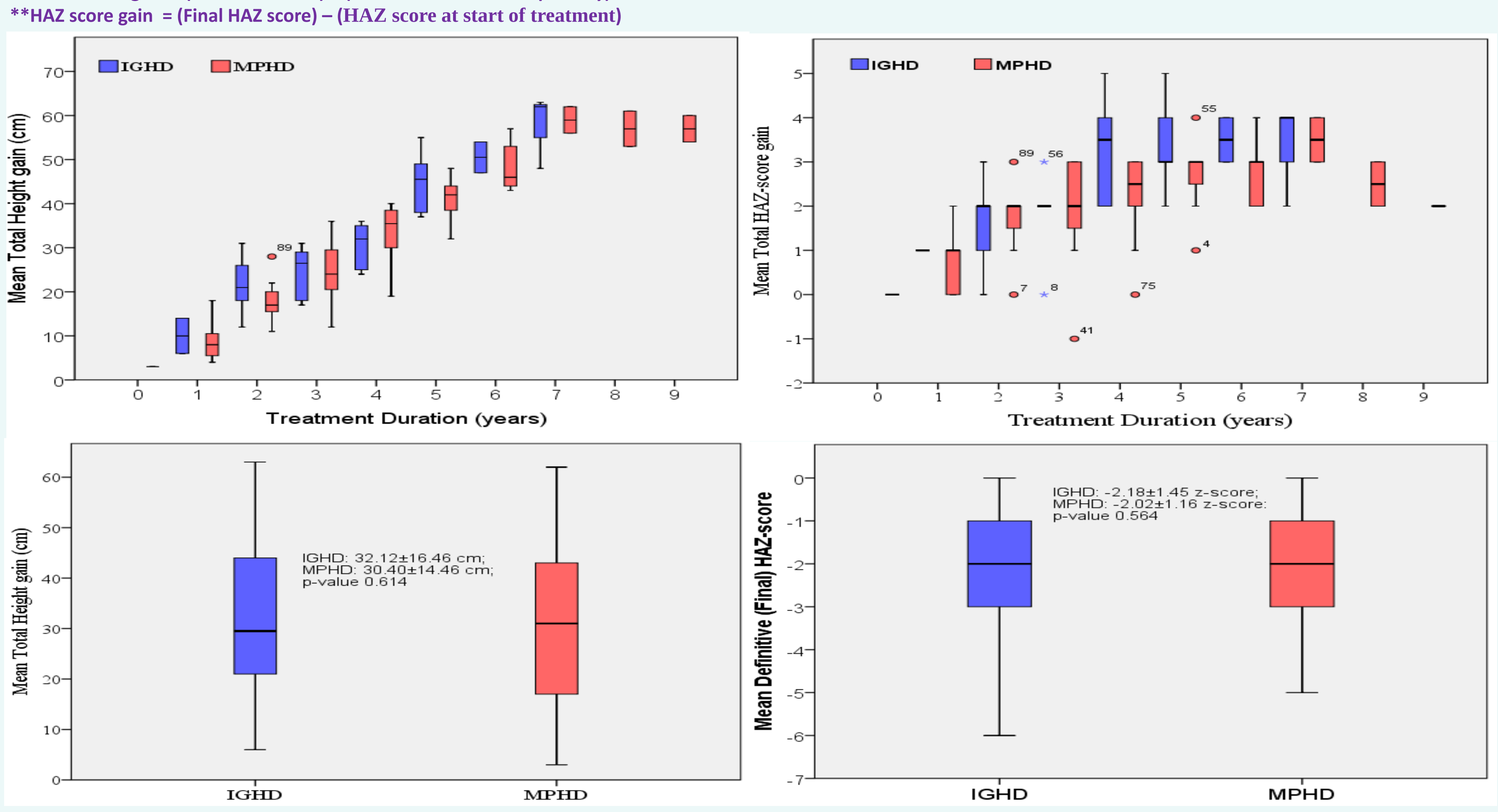
Results

92 patients, who were treated with growth hormone, had attained adult height. The male/female ratio was 70/22.

37% (34/92) of them had IGHD, while 63% (58/92) had multiple pituitary hormone deficiencies. The mean age of starting GH treatment in our patients was 13.06±2.61 years old, with boys starting treatment later (13.21±2.53 years old) compared to girls (12.58±2.87years old).

Table 1. General data		IGHD	MPHD	Total
Gender	Female (no.)	9	13	22
	Male (no.)	25	45	70
Age at starting treatment (years)		13.51±2.13	12.8±2.84	13.06±2.61
HAZ score at start of treatment		-4.59±1.08	-4.10±1.02	-4.28±1.06
Pubertal HAZ gain*		1.99±0.73	1.56±1.07	1.73±0.97
HAZ score gain from start to the end of treatment**		2.47±1.28	2.02±1.13	2.18±1.20
HAZ score at the end of treatment (Final HAZ score)		-2.18±1.45	-2.02±1.16	-2.08±1.27
Duration of treatment (years)		3.73±1.66	3.75±2.16	3.73±1.98
GH dose	**0.21 mg/kg/week (nr)**	21	8	29
	0.24 mg/kg/week (nr)	10	44	54
	0.27 mg/kg/week (nr)	3	6	9

*Pubertal HAZ gain = (Final HAZ score) – (HAZ score at onset of puberty)
**HAZ score gain = (Final HAZ score) – (HAZ score at start of treatment)



Automatic Linear Regression model was built to assess the importance of the variable on the final height. This model noted out that duration of treatment, age at starting of treatment, HAZ score at start of treatment, HAZ score changes during puberty, gender, and Mid Parental HAZ score affects strongly on final height (Table 2).

Table 2. The Importance of linear relationship (GLM) between Predictors and Target (Final Height)							
					95% Confidence Interval		
Model Term	Coef.	Std. Err.	t	**Sig.**	Lower	Upper	**Importance**
Intercept	**68.10**	**16.072**	**4.237**	**.000**	**36.13**	**100.0**	
Duration of treatment	6.454	0.429	15.05	**.000**	5.602	7.307	**0.534**
Age at starting treatment	3.556	0.351	10.13	**.000**	2.858	4.254	**0.242**
HAZ score at start of treatment	5.303	0.629	8.430	**.000**	4.052	6.555	**0.167**
Pubertal HAZ gain	2.934	0.666	3.386	**.001**	1.211	4.657	**0.027**
Gender=Female	-4.93	1.849	-2.67	**.009**	-8.61	-1.25	**0.017**
Mid Parental HAZ score	0.218	0.091	2.395	**.019**	0.037	0.399	**0.014**

Conclusions

Most of our patients with GHD treated with recombinant growth hormone were able to achieve their genetic height potential. Despite starting treatment late, they managed to gain 2.18±1.20 z-scores in height and the final height for majority of them (58.7%) was within the target height range. There was no statistical significance difference between the two main diagnoses, neither in mean of total height gain nor in mean of final (definitive) HAZ-score. It was found that the good Predictors (with greater importance) that had more influence on final height were "duration of treatment with GH"; "age at which GH treatment was started"; "HAZ score at the start of treatment" and the "Pubertal HAZ gain". This study highlighted the importance for early diagnosis and treatment in children with growth hormone deficiency. This is to ensure adequate duration of treatment to optimize the prepubertal growth so that height prognosis of these children can be further improved.

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Growth
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