Severe IGF-I deficiency in children with normal growth hormone (GH) secretion and excluded GH insensitivity – is it really idiopathic short stature?

Joanna Smyczyńska[1], Urszula Smyczyńska[2], Andrzej Lewiński[1,3], Maciej Hilczer[1,4]

[1]Department of Endocrinology and Metabolic Diseases, Polish Mother's Memorial Hospital – Research Institute, Lodz, Poland
[2]Department of Biostatistics and Translational Medicine, Medical University of Lodz, Poland
[3]Department of Endocrinology and Metabolic Diseases, Medical University of Lodz, Poland
[4]Department of Pediatric Endocrinology, Medical University of Lodz, Poland

Authors declare no conflict of interest

Contact: joanna.smyczynska@o2.pl

Introduction

According to current recommendations, children with height SDS <-3.0, normal growth hormone (GH) peak in stimulation tests (stimGH) and severe IGF-I deficiency (IGFD) may be diagnosed with primary IGFD and treated with recombinant IGF-I. The need for direct confirmation of GH insensitivity (GHI) is a matter of discussion. On the other hand, children born small for gestational age (SGA) with no catch-up growth are qualified to GH therapy despite normal GH secretion. The fact that some of them may fulfil the criteria of primary IGFD makes some confusion concerning the optimal treatment for them.

Aim of the study

To test the hypothesis that children with IGFD and excluded GHI may benefit during GH therapy despite normal stimGH and birth size appropriate for gestational age (AGA).

Material and methods

Retrospective analysis comprised **28 children** (23 boys, 5 girls), age 13.0±2.2 years, including **6 cases of SGA and 22 of AGA**, with **height SDS <-3.0, stim GH >10.0 ng/ml** (after falling asleep and/or in at least in one of the pharmacological stimulation tests - with clonidine and with glucagon) **and severe IGFD** (defined as **IGF-I SDS** for age and sex **<-2.0**).

In each case, **IGF-I generation test** (IGF-GT) was performed with GH dose 0.033 mg/kg/day for 7 days. GHI was as excluded by **significant IGF-I increase** in IGF-GT, defined arbitrarily as IGF-I concentration at the end of the test within normal range together with at least doubling the initial value of IGF-I level.

The **patients were treated with GH** in standard doses for GHD **up to final height (FH)**.

The pre-treatment characteristics and the efficacy of treatment were compared between SGA and AGA.

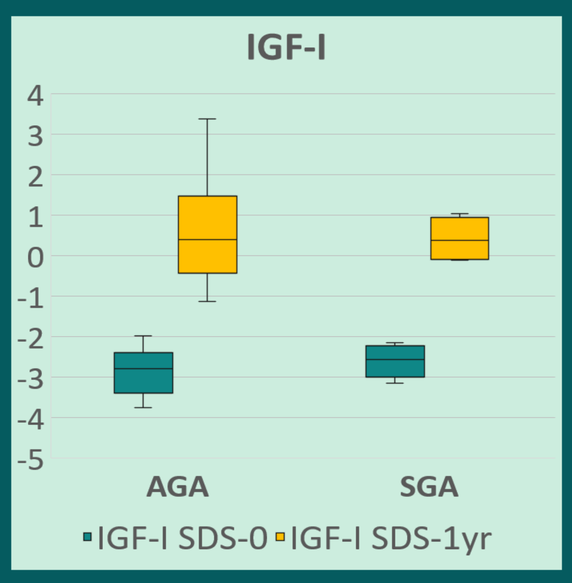
Results

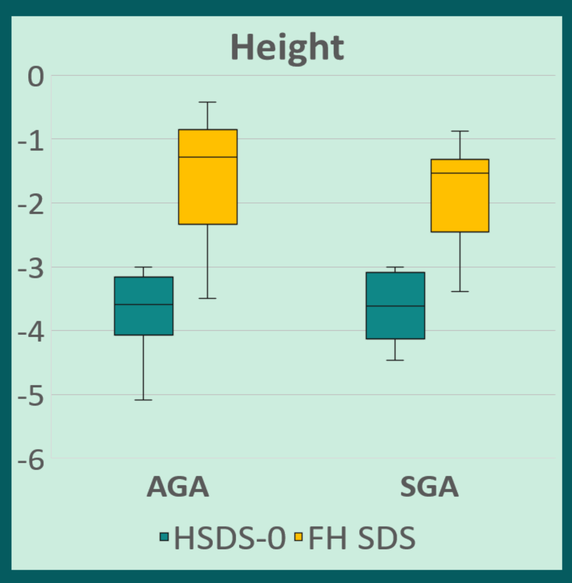
	SGA	AGA	p
Age at diagnostics [years]	12.4±2.5	13.2±2.1	0.76
Height SDS pre-treatment (HSDS-0)	-3.64±0.59	-3.79±0.88	0.89
HSDS-0 corrected vs. target height SDS	-3.12±1.06	-2.48±1.16	0.13
Height velocity (HV) before treatment [cm/year]	3.4±1.0	3.8±0.8	0.34
Bone age delay (BA/CA ratio)	0.74±0.11	0.80±0.09	0.24
GH peak in stimulation tests (stimGH) [μg/l]	14.7±8.6	19.6±9.4	0.11
IGF-I SDS before IGF-GT (IGF-I SDS-0)	-2.60±0.39	-3.08±0.98	0.37
IGF-I SDS at the end of IGF-GT	-0.19±0.62	-0.40±1.13	0.76
IGF-I SDS increase during IGF-GT	2.41±0.67	2.68±0.77	0.49
Height velocity (HV) in 1st year of therapy [cm/year]	7.2±2.2	8.6±3.3	0.18
HV increase in 1st year of therapy [cm/year]	3.7±2.7	4.2±2.5	0.59
IGF-I SDS in 1st year of therapy (IGF-I SDS-1yr)	0.42±0.52	0.56±1.56	0.92
GH therapy duration [years]	5.2±3.1	4.1±1.3	0.71
Final height SDS (FH SDS)	-1.82±0.87	-1.66±0.94	0.53
FH SDS corrected vs. target height SDS	-1.31±1.03	-0.35±1.02	0.09
Increase of FH SDS vs. HSDS-0 (Δ hSDS)	1.81±0.53	2.13±0.99	0.37

There was no significant difference between SGA and AGA children in: pre-treatment height SDS, pre-treatment height velocity (HV), stim GH, IGF-I SDS, both before IGF-GT and after 7 days of GH administration.

During 1st year of treatment, in AGA and SGA similar increase was observed for HV and IGF-I SDS.

The attained FH SDS was even better in AGA than in SGA, similarly as the increase of FH SDS vs. pre-treatment height SDS.





Conclusions

It seems that children with height SDS <-3.0, normal stimGH and severe IGFD should not be diagnosed with primary IGFD if GH insensitivity is not documented.

In case of AGA, they should not also be diagnosed with idiopathic short stature and remain untreated, as they may benefit during GH therapy at least similarly to SGA ones.