

GROWTH HORMONE TREATMENT IN CHILDREN BORN SMALL FOR GESTATIONAL AGE (SGA)



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No conflict of interests

Introduction and objectives

- **SGA (small for gestational age)** - are children born with **birth weight and/or length (BW/ BL) under two standard deviations (< 2 SD)** for the gestational age and sex of the population [1, 2];
- **The prevalence** of these children - **between 2.3% to 10% worldwide** [1, 2];
- SGA born children **have health consequences throughout their whole life** [2];
- **Growth failure** - the **most common consequence** in small for gestational age (SGA) children [2, 3, 4].
- Approximately **5÷10 % of them do not achieve catch-up growth and remain short after 4th year of age** [3, 4];
- The **potential risk of short stature in adulthood** – **5÷7 times higher in children born SGA** than in their peers born appropriate for their gestational age, AGA [5];

Abstract

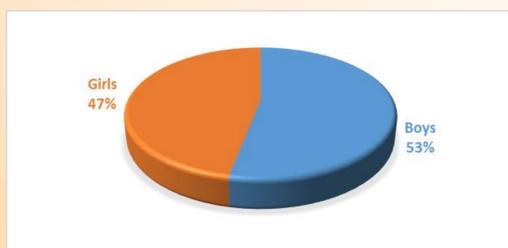
Introduction: Growth failure is a common consequence in small for gestational age (SGA) children.
Patients and Methods: The growth patterns and serum insulin like growth factor 1 (IGF1) concentrations before and after the 1st year under growth hormone treatment of 32 short stature SGA born children have been evaluated. In addition, we investigated the insulin like growth factor 1 receptor (IGF1R) exon 2 as a hotspot for IGF1R genetic alterations. It is of note that no dysmorphic features were observed in this group of children.
Results: The tests for pituitary reserve were within normal ranges for all 32 patients. Growth hormone (GH) treatment (0.037mg/kg/day) was initiated at the mean age of 9.32±3.19 years. Growth velocity increased yearly from -1.80 SDS after the first year to -0.03 SDS at the sixth year of treatment. Their IGF1 serum concentrations before treatment were age and sex appropriate, while during treatment a significant increase was observed fitting in the upper third of the normal range: before the treatment IGF1 SDS was 0.84±1.78 after 1st year the concentrations increased to IGF1 SDS 0.94±2.23. No genetic alterations were found in the IGF1R exon 2 by PCR analysis.
Conclusions: Herein we present 32 short stature SGA children with no dysmorphic features treated with GH. They all had increased growth velocity and entered the normal growth range on their growth charts. No side-effects were observed. GH treatment in children with no genetic alterations on the IGF1R exon 2 is safe and efficient in treating SGA children with short stature.
Key words: small for gestational age, short stature, IGF1, insulin like growth factor 1 receptor, growth hormone treatment

Methods

- **Clinical data:**
✓ birth weight (BW) in kilograms, birth length (BL) in centimeters, BW standard deviation score (SDS), BL SDS and gestation weeks (GW);
- **Growth parameters:**
✓ Height SDS, weight SDS, body mass index (BMI), BMI z-score, occipitofrontal circumference/OFC SDS and target height SDS;

- **The serum concentrations of IGF1 were determined by:**
✓ Chemi-luminescence immune assay method (IMMULITE 2000 Siemens, Immunoassay System apparatus);
- **The molecular analysis of IGF1R exon 2:**
✓ The exon 2 was amplified with the following primers:
5'TCGACATCCGCAACGACTATC3' - the forward primer and
5'CGAAGATGACCAGGGCGTAG3' - the reverse primer;
✓ PCR restriction-site analysis and followed by direct sequencing of conspicuous fragments;

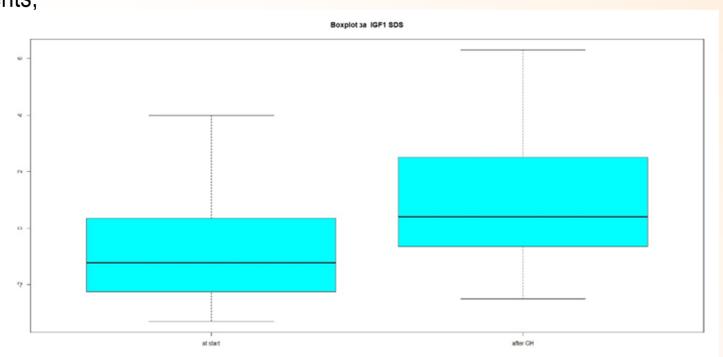
Results



- ❖ No dysmorphic features in SGA born children;
- ❖ Average age of 9.32±3.19 ys at the start of the study;
- ❖ The mean bone age delay - 2.77±0.47 SDS years;
- ❖ The tests for pituitary reserve - within normal ranges;
- ❖ GH treatment - 0,037mg/daily dose in all patients;
- ❖ IGF1 SDS - 0.84±1.78 at start, after 1st year of GH treatment - increased to 0.94±2.23;
- ❖ No genetic alterations were found in the IGF1R exon 2 by PCR analysis;

PARAMETERS	GROUP	short SGA children mean
H SDS	-	-2.77 ±0.72 SDS
W SDS	-	-1.84 ±0.83 SDS
BMI	kg/m ²	15.44 ±2.01 SDS
BMI z-score	-	-0.97 ±2.03 SDS
OFC SDS	-	-0.86 ±1.27 SDS
TH SDS	-	-1.16 ±0.76 SDS

PARAMETERS	GROUP	short SGA children mean
BW	gr	2254.00 ±392.27 SDS
BW SDS	-	-2.78 ±0.90 SDS
BL	cm	46.87 ±2.19 SDS
BL SDS	-	-1.37 ±0.86 SDS
GW	w	39.06 ±1.04 SDS
Patients	M	n= 17
	F	n= 15

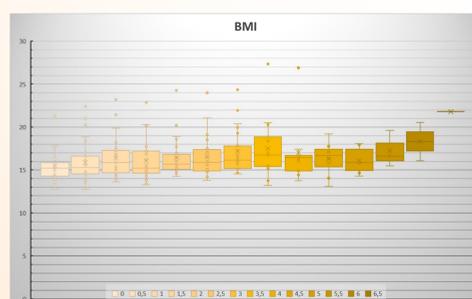
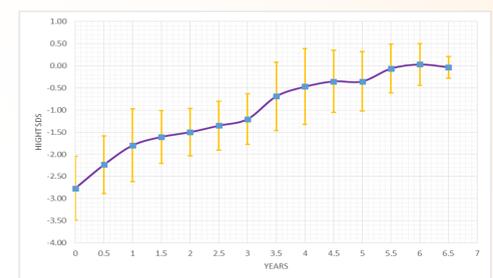
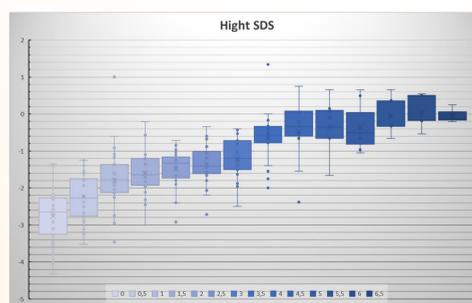


Discussion

- ✓ Majority of SGA born children are not growth hormone (GH) deficient [6, 7];
- ✓ GH treatment in SGA children has been approved in USA and EU - after 2nd year of age – FDA and after 4th year of age – EMEA [8];
- ✓ **Safeness and Effectiveness** of the GH treatment;
- ✓ **Time of onset** - before puberty - very important predictor for the height achievement;
- ✓ **A start of treatment even 1 year before puberty is beneficial, but greater effect has been achieved if treatment was initiated two years before puberty;**
- ✓ **Consensus Statement** in 2007y - an early initiation with GH treatment in SGA children with severe growth retardation (<-2.5 SDS) aged between 2 and 4 year [2];
- ✓ **The important role of the GH and IGF1 on brain development and linear growth** - GH commencement before 2 year of age [9];
- ✓ **Decreasing the frequency metabolic complications** - in adolescence and adulthood;
- ✓ **Multidisciplinary approach** - perinatologist, nutritionist and pediatric endocrinologist

Conclusions

- An adequate growth monitoring during childhood, an early assessment of short stature and timely treatment can prevent the short adult stature in this group of children;
- Herein we present 32 short stature SGA children with no dysmorphic features treated with GH.
- They all had increased growth velocity and entered the normal growth range on their growth charts.
- No side-effects were observed.
- GH treatment in children with no genetic alterations on the IGF1R exon 2 is safe and efficient in treating SGA children with short stature.



References

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