

# Do IGF-I Generation Test Results Predict First Year Growth Response to GH Treatment in Idiopathic Short Stature?

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## BACKGROUND AND OBJECTIVE

### Background:

It is well-known that human growth hormone (hGH) treatment increases growth rate in idiopathic short stature (ISS) in the short term which might predict the overall height gain. However, the fact that ISS might involve a heterogeneous group of individuals with individual benefits from hGH treatment makes the decision to treat or not to treat difficult. There is some evidence in the literature suggesting an IGF generation test might be a tool for distinguishing ISS individuals who would benefit from hGH treatment(2,3).

### Objective :

The aim of this study was to investigate retrospectively whether an IGF-I generation test( IGFGT) might be used as a tool to predict the first year growth response to GH treatment in individuals with ISS.

## METHODS

Fifty seven subjects with ISS who had at least %20 increase in IGF-I levels with an IGFGT and who were treated for at least one whole year with GH were included in the study. Of these 57 subjects, 29 were girls. The mean age of the patients was  $11,47 \pm 1,95$  years and 38 were prepubertal. Blood samples for IGF-I concentration measurements were collected in morning hours, before the 1st rhGH injection(first day) and on the 5th day after 4 daily doses of 0,033 mg/kg (0,1 IU/kg). IGF-I levels were measured by a chemiluminescence immunoassay. IGF-I levels and heights were expressed as SDS both for age and gender(1). Bone age was evaluated by Greulich Pyle method. The increase in IGF-I levels were expressed both as the percentage of the initial value and delta IGF SDS.

## RESULTS

Height SDS increased significantly both in pubertal and prepubertal subjects; however, bone age increased  $2,12 \pm 1,54$  years and  $2,00 \pm 1,32$  years in one year respectively(Tables 1 and 2).

Pubertal Group (n=19)			
	Before	After	p
Decimal Age(year)	$13,03 \pm 1,30$	$14,13 \pm 1,23$	0,000
Height SDS	$-2,78 \pm 0,88$	$-2,03 \pm 0,80$	0,000
Growth velocity (cm/year)	$5,18 \pm 1,66$	$8,08 \pm 2,20$	0,003
Bone Age (year)	$11,26 \pm 1,62$	$13,08 \pm 1,44$	0,000
Weight SDS	$-1,79 \pm 1,03$	$-1,65 \pm 0,95$	0,186
Body Mass Index (kg/m <sup>2</sup> )	$17,54 \pm 3,58$	$18,18 \pm 3,29$	0,009

Table 1- Auxological characteristics in pubertal patients before and after 1 year of growth hormone treatment

Prepubertal Group (n=38)			
	Before	After	P
Decimal Age (year)	$10,69 \pm 1,76$	$11,74 \pm 1,73$	0,000
Height SDS	$-2,77 \pm 0,54$	$-2,50 \pm 0,64$	0,000
Growth velocity (cm/year)	$4,07 \pm 1,44$	$7,29 \pm 1,52$	0,000
Bone Age (year)	$7,69 \pm 1,98$	$9,63 \pm 2,43$	0,000
Weight SDS	$-1,76 \pm 0,51$	$-1,69 \pm 0,55$	0,109
Body Mass Index (kg/m <sup>2</sup> )	$15,37 \pm 1,97$	$16,20 \pm 2,35$	0,004

Table 2- Auxological characteristics in prepubertal patients before and after 1 year of growth hormone treatment

In the prepubertal group both basal and stimulated IGF-I SDS were higher than those in the pubertal group. However,  $\Delta$ IGF-I SDS in the pubertal group was significantly higher than in the prepubertal group(Table 3). Although bone age SDS and weight SDS were similarly affected in prepubertal and pubertal children, delta height SDS was significantly higher in the pubertal group than in the prepubertal group(Table 4).

	Prepubertal Group (n=38)	Pubertal Group (n=19)	p	
Growth Hormone peak (ng/ml)	$16,38 \pm 6,79$	$14,47 \pm 3,38$	0,253	
IGF-1 SDS	Basal	$-2,46 \pm 1,02$	$-4,20 \pm 1,48$	0,000
	Stimulated	$-1,47 \pm 1,17$	$-2,48 \pm 1,65$	0,010
$\Delta$ IGF-1 SDS	$0,99 \pm 0,5$	$1,72 \pm 0,92$	0,000	
Increase in IGF-1(%)	$79,95 \pm 46,01$	$94,09 \pm 156,45$	0,607	

Table 3- The comparison of growth hormone peak levels and basal and stimulated IGF-1 SDS levels and results of IGF-1 generation test( $\Delta$  adn %) between the prepubertal and pubertal groups

	Prepubertal Group (n=38)	Pubertal Group (n=19)	p	
Height SDS	Before	$-2,77 \pm 0,54$	$-2,78 \pm 0,88$	0,964
	After	$-2,50 \pm 0,64$	$-2,03 \pm 0,80$	0,020
$\Delta$ Height SDS		$0,27 \pm 0,33$	$0,74 \pm 0,45$	0,000
Weight SDS	Before	$-1,76 \pm 0,51$	$-1,79 \pm 1,03$	0,887
	After	$-1,69 \pm 0,55$	$-1,65 \pm 0,95$	0,83
$\Delta$ Weight SDS		$0,07 \pm 0,25$	$0,14 \pm 0,44$	0,466
$\Delta$ Bone Age (year)	$2,00 \pm 1,32$ (n=32)	$2,12 \pm 1,54$ (n=15)	0,865	

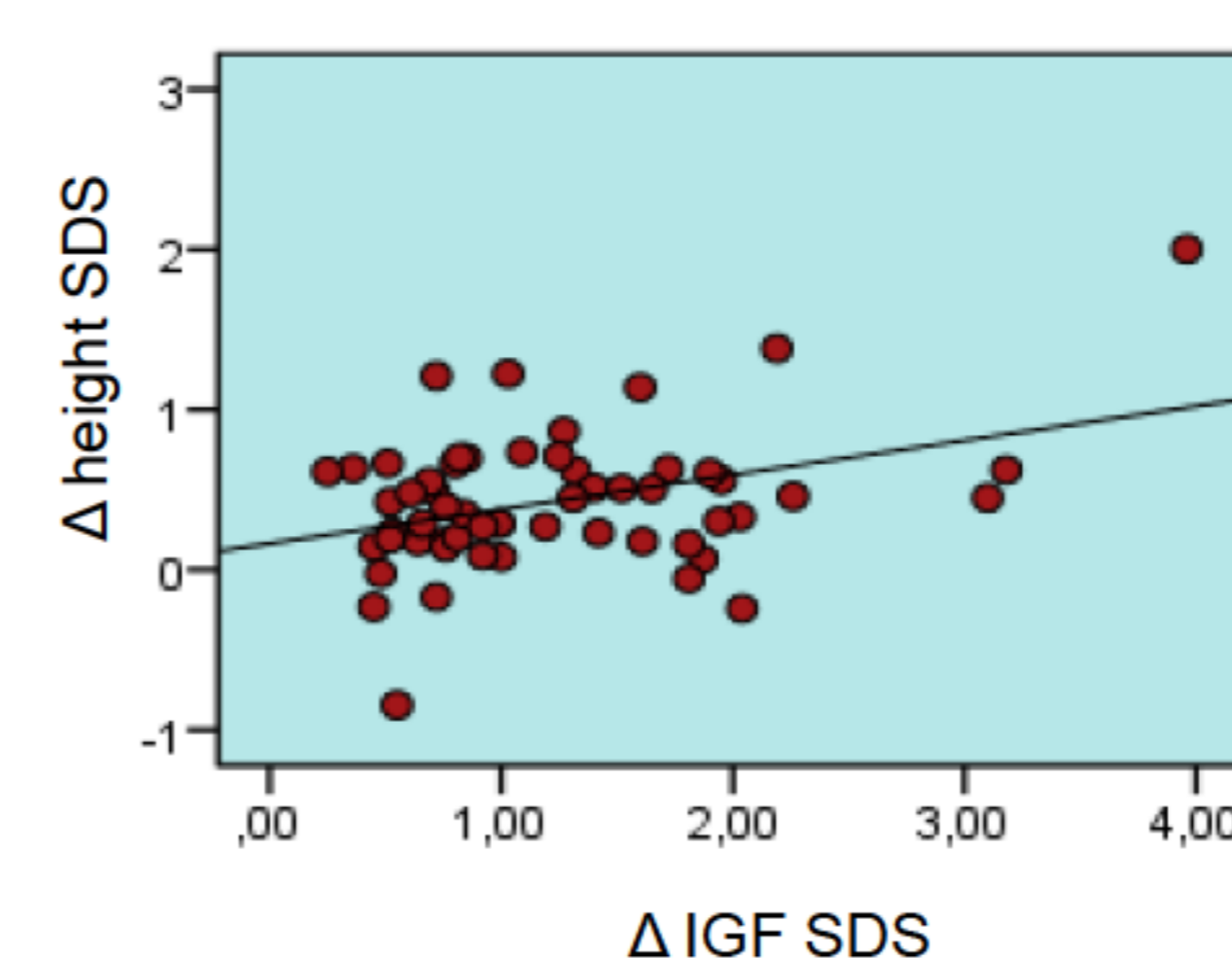
Table 4- The comparison of the effect of treatment on auxological parameters between the prepubertal and pubertal groups

## CONCLUSION

Our results suggest that in individuals with ISS, the lower basal IGF-I SDS is and the higher increase in IGF-I SDS (in an IGFGT) is, the more the height gain after one year of GH treatment is. Our findings might be explained by a recent observation which indicates that the degree of the individual IGF-I response to GH in childhood and thus individual growth hormone sensitivity is modulated by genetic and epigenetic variation at the GHR and IGF-I loci(4).

## REFERENCES

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There was a negative correlation between delta height SDS and basal IGF-I SDS ( $r=-0,434$ ,  $p=0,001$ ). As can be seen in Figure 1, there was a positive correlation between delta height SDS and delta IGF-I SDS ( $r=0,372$ ,  $p=0,004$ ) but the same was not true for percentage increase in IGF-I

Figure 1- The relationship between delta IGF SDS and delta height SDS

