

# Metabolic effects of growth hormone treatment in short prepubertal children: a double-blinded randomized clinical trial

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## Objective

To investigate the metabolic effects of various doses of recombinant human growth hormone (rhGH) in short prepubertal children with stimulated growth hormone (GH) peak levels in the lower normal range (7-14 µg/L).

## Method

Thirty-five prepubertal short children (<-2.5 SDS), aged 7-10 years, with peak levels of GH between 7 and 14 µg/L in an arginine insulin tolerance test (AITT), were randomized to three different doses (11/33/100 µg/kg/d) of rhGH treatment for two years.

The doses were blinded for both patients and study investigators.

Auxological and different metabolic investigations were performed, including metabolites in blood and interstitial microdialysis fluid, dual-energy X-ray absorptiometry (DEXA), frequently sampled intravenous glucose tolerance test (FSIVGTT) and stable isotope examinations of rates of glucose production and lipolysis.

## Results

At 24 months, the high dose group had higher fasting insulin, higher acute insulin response (AIR) in the FSIVGTT, and was more insulin resistant in the homeostasis model assessment of insulin resistance (HOMA-IR) compared with the standard and low dose groups. Few other metabolic differences were found at the end of the study, but a decreased insulin sensitivity index (Si) measured by FSIVGTT could be seen already at 12 months for both the standard and high dose groups compared with the low dose group.

A selection of metabolic outcome variables and comparisons between the groups are presented to the right (Table 1) as well as a figure illustrating changes in certain auxological and metabolic parameters over the two-year study period within each group (Figure 1a-f).

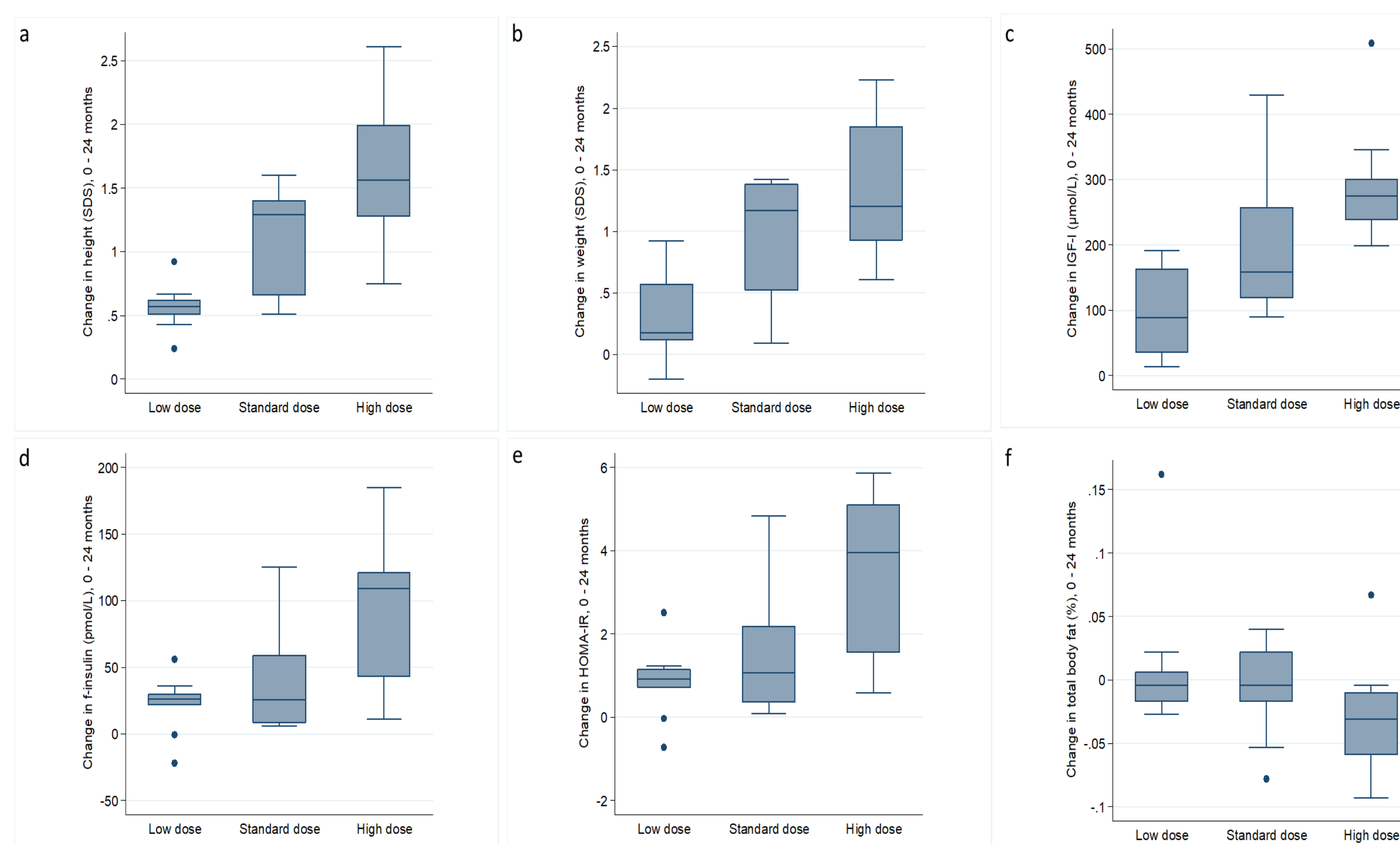
## Conclusion

A clear dose-dependent effect of GH treatment on several metabolic parameters was found, particularly for the high dose group regarding fasting insulin levels and indices of insulin resistance.

**Table 1.** Comparison of metabolic parameters at 12 and 24 months

	Low dose (11µg/kg/d)	Standard dose (33µg/kg/d)	High dose (100µg/kg/d)	p-values		
				Low vs Standard	Standard vs High	Low vs High
<b>12 months</b>						
F-insulin (pmol/L)	52.5 (36.4)	43.5 (26.4)	74.7 (36.9)	N.S.	N.S.	N.S.
IGF-I (µg/L)	197 (98)	242 (62)	352 (121)	N.S.	<0.001	<0.001
HOMA-IR	1.99 (1.61)	1.51 (0.95)	2.77 (1.48)	N.S.	0.006	N.S.
HOMA2-IR	1.00 (0.70)	0.83 (0.49)	1.43 (0.72)	N.S.	0.012	N.S.
Si ([mU/l] <sup>-1</sup> x min <sup>-1</sup> )	10.1 (2.5)	6.4 (1.7)	5.4 (1.8)	0.025	N.S.	0.003
AIR (mUxL <sup>-1</sup> x min)	271 (203)	395 (300)	509 (264)	N.S.	N.S.	0.026
Tot. fat mass (%)	16.9 (6.2)	14.2 (6.1)	11.0 (4.8)	N.S.	N.S.	0.035
<b>24 months</b>						
F-insulin (pmol/L)	46.0 (22.9)	61.2 (35.8)	111.7 (52.9)	N.S.	<0.001	<0.001
IGF-I (µg/L)	220 (106)	291 (105)	402 (114)	0.007	0.002	<0.001
HOMA-IR	1.71 (0.93)	2.17 (1.38)	4.20 (1.94)	N.S.	<0.001	<0.001
HOMA2-IR	0.89 (0.44)	1.17 (0.69)	2.13 (0.96)	N.S.	<0.001	<0.001
Si ([mU/l] <sup>-1</sup> x min <sup>-1</sup> )	7.9 (2.0)	7.8 (2.9)	5.2 (2.5)	N.S.	N.S.	N.S.
AIR (mUxL <sup>-1</sup> x min)	348 (229)	418 (337)	667 (388)	N.S.	0.035	0.009
Total fat mass (%)	17.2 (9.6)	15.8 (6.3)	12.9 (6.3)	N.S.	N.S.	N.S.

Note: Mean (SD). IGF-I = insulin-like growth factor I, HOMA-IR/HOMA2-IR = homeostasis model assessment of insulin resistance, Si = (insulin) sensitivity index (measured by frequently sampled intravenous glucose tolerance test), AIR = acute insulin response (measured by frequently sampled intravenous glucose tolerance test), N.S. = non-significant.



**Figure 1a-f:** Changes in auxological and metabolic outcomes over the study period

The box-plots (a-f) show changes from baseline to the end of the study period ( $\Delta$ -values, 0-24 months) for the three treatment groups in different auxological and metabolic parameters.

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