Prediction of the first-year response to growth hormone treatment in prepubertal Korean children with idiopathic growth hormone deficiency: analysis of data from the LG Growth Study database

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Background: Insufficient data exist for the prediction of the first-year response to growth hormone (GH) treatment in Korean prepubertal children with idiopathic GH deficiency (GHD).

Subjects: The LG Growth Study (LGS) is a long-term observational cohort study and non-interventional registry evaluating the long-term safety and effectiveness of recombinant human growth hormone Eutropin inj., Eutropin AQ inj. (LG Chem, Korea) in Korean children and on-going study, and new patients are continually being recruited.

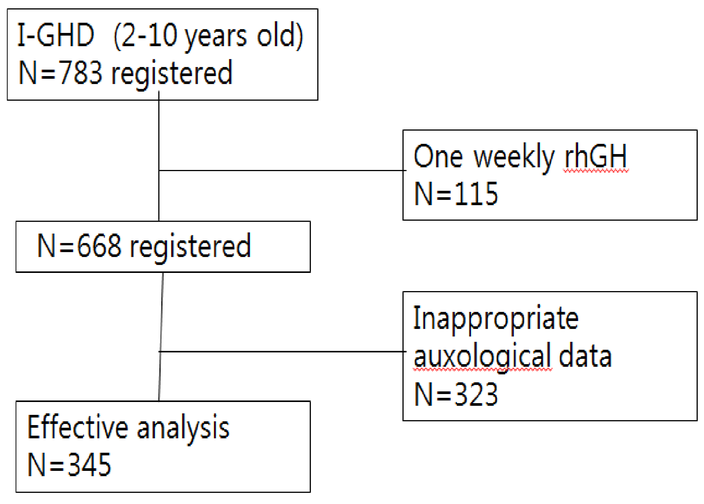

Fig.1. A flow chart of cohort. Data from children (n=345) in the LGS (LG Growth Study Database), or who had participated in clinical trials were used to develop the model. All included patients were diagnosed as idiopathic GH deficiency with maximum GH levels within at least 2 GH stimulation tests < 10 ng/ml, and prepuberty during the first year of GH treatment. Children with pituitary/hypothalamic lesions were excluded.

Statistical analysis: The prediction model for growth response (△height SDS) during the initial year of GH therapy was developed using a multiple linear regression analysis fitted by least squares and the REG procedure in the SAS® version 9.4 (SAS Institute, Inc., Cary, NC, USA).

A hierarchy of predictive factors was derived by the all-possible regression approach, using Mallow's C(p) criterion for ordering predictive factors, as described previously

RESULTS

Table 1. Characteristics of the study group.

	IGHD (n=345)
Gender, Male, n (%)	195 (56.52%)
Age (years) at start of GH (n=345)	6.12 (2.24 ,9.97)
Height SDS (n=345)	-2.56 (-7.96 ,-1.9)
Weight SDS (n=280)	-2.04 (-7.89 ,1.03)
BMI SDS (n=277)	-0.37 (-3.92 ,3.57)
Bone age (years) (n=309)	4 (0.6 ,12.5)
Father Height (cm) (n=308)	170 (145 ,184)
Father Height SDS (n =308)	-0.6 (-5.27 ,1.85)
Mother Height (cm) (n =309)	156 (142 ,171)
Mother Height SDS (n =309)	-0.96 (-4.05 ,1.94)
MPH (cm) (n=308)	164.5 (144 ,179)
MPH SDS (n=308)	-0.78 (-3.92 ,1.11)
GH initial dose (mg/kg/week) (n=280)	0.23 (0.03 ,0.5)
Maximum GH serum levels in stimulation tests (n=345)	6.97 (0.06 ,9.99)
IGF-1 (n=289)	111 (2.9 ,607)
IGF-1-SDS (n=289)	-0.83 (-2.68 ,5.32)
IGFBP-3 (n=263)	2380 (755 ,6520)
IGFBP-3-SDS (n=263)	-0.21 (-3.83 ,6.69)
PAH (n=298)	167.69 (134.02 ,219.21)
PAH SDS (n=298)	-0.02 (-6.01 ,7.59)
MPH SDS – height SDS (n=308)	1.81 (-1.73 ,7.81)
HV (n=345)	8.99 (3.18 ,15.45)
△Height SDS (n=345)	0.84 (-0.39 ,2.98)

Abbreviations: GH, growth hormone; SDS, standard deviation score for chronological age; BMI, body mass index, MPH, mid parental height; HV, Height velocity; △Height SDS, Change in height standard deviation score between before and after 1 year GH treatment. IGF-I, insulin-like growth factor-I; IGFBP-3, insulin-like growth factor binding protein-3; BMI, body mass index; PAH, predicted adult height

CONCLUSION

In Korean prepubertal children with idiopathic GHD, the first-year response to GH treatment was negatively correlated with chronological age and positively correlated with BMI and the difference between their MPH SDS and a child's present height SDS.

Table 2. Simple regression analysis between delta height SDS and characteristic and laboratory data in prepubertal Korean children with idiopathic GHD

IGHD (N=345)	n	R-squre	β	p-value
Age (years) at start of GH	345	0.1159	-0.294	<.0001
Height SDS	345	0.0005	0.045	0.6889
Weight SDS	280	0.0455	0.304	0.0003
BMI SDS	277	0.1006	0.443	<.0001
Bone age (years)	309	0.0901	-0.249	<.0001
Father Height SDS	308	0.0333	0.296	0.0013
Mother Height SDS	309	0.0114	0.152	0.0612
MPH (cm)	308	0.0159	0.026	0.0268
MPH SDS	308	0.0398	0.421	0.0004
GH initial dose(mg/kg/week)	280	0.0086	-2.188	0.1214
Maximum GH serum levels in stimulation tests (n=345)	345	0.0060	-0.055	0.1511
IGF-1	289	0.0066	-0.002	0.1670
IGF-1-SDS	289	0.0057	0.124	0.1989
IGFBP-3	263	0.0046	0.000	0.2726
IGFBP-3-SDS	263	0.0001	0.007	0.8769
PAH	298	0.0097	0.013	0.0902
PAH SDS	298	0.0117	0.094	0.0627
MPH SDS – height SDS	308	0.071	0.09857	<.0001

Abbreviations: GH, growth hormone; SDS, standard deviation score for chronological age; BMI, body mass index; MPH, mid parental height; HV, Height velocity; △Height SDS, Change in height standard deviation score between before and after 1 year GH treatment. IGF-I, insulin-like growth factor-I; IGFBP-3, insulin-like growth factor binding protein-3; BMI, body mass index; PAH, predicted adult height

Table 3. Prediction model of △Height SDS during 1st year of GH treatment in prepubertal Korean children with idiopathic GHD (N=345).

IGHD	Parameter estimate	Rank of predictor	Partial Variability (R^2x100)	P-value	Variance Inflation
Intercept	1.06			<.0001	0
Age (years) at start of GH	-0.05	1	12.77	<.0001	1.10448
MPH SDS – height SDS	0.09	2	5.09	0.0002	1.01768
BMI SDS	0.05	3	1.71	0.0145	1.09293
Total explained variability (R^2x100)			19.57		
Error SD			0.31		

Abbreviations: GHD, growth hormone deficiency; IGHD, Idiopathic GHD; MPH, mid parental height; SDS, standard deviation score for chronological age; BMI, body mass index; △Height SDS, Change in height SDS between before and after 1 year GH treatment; Error SD, Standard deviation of error. The estimated regression equation is as follows △Height SDS during 1st year of GH treatment= 1.06 - 0.05 * age + 0.09 * (MPH SDS – height SDS) + 0.05 * BMI SDS

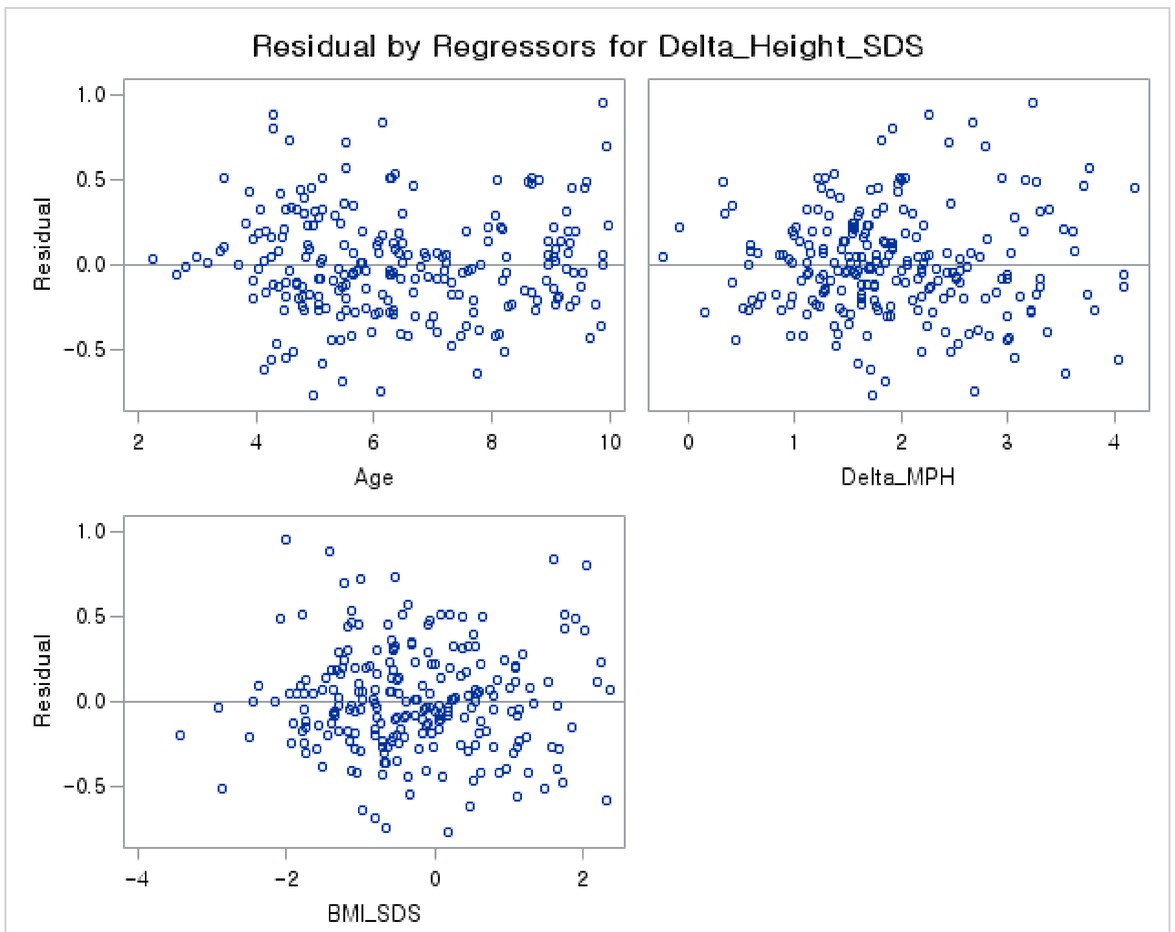

Fig.2. Studentized residuals for Prediction model of △Height SDS during 1st year of GH treatment in prepubertal Korean children with idiopathic GHD. The studentized residual and predicted value graphs in the conformity assessment graph used in the validation of prediction models were distributed randomly between −2 and 2, and there were no values outside −3 and 3.