Original Article

Recombinant growth hormone improves growth and adult height: a comparison between treated and untreated patients with idiopathic growth hormone deficiency

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Background: Recombinant human growth hormone (rhGH) is a standard treatment for idiopathic growth hormone deficiency (IGHD) patients to normalize growth. Prior studies on children mainly focused on short-term growth velocity effects, with limited long-term data on adult height outcomes. This study aims to assess adult height outcomes in patients with and without rhGH treatment, as well as evaluate the efficacy of rhGH treatment in individuals with IGHD.

Methods: A total of 169 individuals with IGHD who had attained their adult height were recruited. The related clinical and laboratory data, including anthropometric parameters, insulin-like growth factor-1 (IGF-1) levels, and the peak growth hormone (GH) levels, were collected. To assess the effectiveness of rhGH treatment, we evaluated the increase in final adult height and height standard deviation score (SDS).

Results: The final adult height SDS was −0.78 (interquartile range: −1.78 to 0.45) in the rhGH untreated group and −0.45 (interquartile range: −1.13 to 0.05) in the rhGH-treated group. The study results revealed that, in the IGHD population, the final adult height SDS and the increase in height SDS in the rhGH treatment group were significantly greater than those in the untreated group ($P<0.05$). Furthermore, the results of multiple regression analysis showed a significant increase in adult height SDS in patients treated with rhGH compared to those not treated with rhGH ($\beta=0.41$, 95% confidence interval: 0.14, 0.69; $P=0.003$) in the IGHD population. The baseline height SDS, peak GH, and rhGH treatment significantly affected the final adult height and height SDS gain in the IGHD population.

Conclusions: Our findings demonstrate that rhGH treatment effectively improves the final height SDS and height SDS gain in children with IGHD.

Keywords: Recombinant human growth hormone (rhGH); cohort study; short stature; growth outcome; final adult height

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Introduction

Growth is one of the most crucial physiological processes during childhood, which depends on the coordinated action of various endocrine hormones, nutrients, and genetic factors. Among these hormones, growth hormone (GH) plays a central role in promoting bone growth and muscle development, and regulating metabolism (1). Idiopathic growth hormone deficiency (IGHD) is a common endocrine disorder, characterized by insufficient secretion of GH in children without a clear cause (2). Its main clinical manifestations include growth retardation, short stature, and delayed bone age. The height of these children is usually more than 2 standard deviations below the average height of normal children of the same age and sex, which severely affects their physical development and mental health (3). As they grow older, short stature may cause these children to face many difficulties in social interaction, education, and career choices, reducing their quality of life and social integration (4,5), with studies showing that short children have significantly lower quality of life scores than children of normal height (6-8).

Since the 1980s, recombinant human growth hormone (rhGH) has been gradually and widely used in the clinical treatment of GHD. Its therapeutic principle is to supplement the deficient GH in children, stimulate the proliferation and differentiation of chondrocytes in the bone growth plate, and thus promote height growth (9). The reason for deciding to use rhGH is based on considering the consequences that may result from short stature. Despite short stature often indicating underlying issues, it is not a standalone disease. Severe short stature can pose as a physical impediment, yet the physical repercussions of mild to moderate short stature remain inconclusive. The goal of rhGH therapy is to expedite the normalization of height and attain a satisfactory adult stature. Research findings demonstrate the efficacy of rhGH treatment in enhancing adult height, with a significant increase in height observed throughout the course of treatment (10). In addition to regulating linear growth in childhood, rhGH also influences the metabolism of fats, proteins, and carbohydrates, as well as impacts the cardiovascular system (11).

rhGH therapy is recognized for enhancing the stature of individuals with short stature. However, previous studies (12,13) on the effectiveness of rhGH focused on improving height in short stature patients who received rhGH treatment, while there was insufficient follow-up for those who did not receive rhGH treatment. With increasing age, especially the emergence of puberty, the height of children and adolescents will be improved to varying degrees (14).

Currently, a sufficiently large sample size and long-term follow-up data on the long-term effects of rhGH treatment for IGHD, especially its impact on adult height, are lacking. Understanding the specific improvement in growth and adult height in children with IGHD after rhGH treatment is highly important for clinicians to formulate reasonable treatment plans, evaluate treatment effects, and provide accurate prognostic information to parents. Moreover, by comparing the growth status of treated and untreated children, the therapeutic value of rhGH can be evaluated more objectively, providing a scientific basis for further optimizing treatment strategies. Therefore, the objective of this study was to examine the adult height outcomes in individuals with and without rhGH treatment, and to evaluate the effectiveness of rhGH therapy in individuals with IGHD. We present this article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-2024-576/rc).

Highlight box

Key findings

- In patients with idiopathic growth hormone deficiency (IGHD), those treated with recombinant human growth hormone (rhGH) exhibited a significant increase in final adult height and height standard deviation compared to the untreated group.

What is known and what is new?

- Patients with IGHD present with short stature in childhood and an increased risk of cardiovascular disease in the long term. rhGH therapy improves height in patients with short stature, but there is a lack of data on long-term follow-up of rhGH therapy especially to reach adult lifetime height.
- The innovations of this study are its examination of the final adult height obtained in children with IGHD and its inclusion of children with IGHD who achieved natural growth without rhGH treatment. The study results provide useful information for the treatment strategies of patients with IGHD in China.

What is the implication, and what should change now?

- Our study provides new evidence for the effect of rhGH treatment on adult height in children with IGHD.

Methods

Participants

A total of 169 participants with IGHD were recruited between March 2013 and March 2021 at the Endocrinology

Department of the Affiliated Hospital of Jining Medical University. These individuals were involved in the GDDSD research project, which is an ongoing prospective, observational, open cohort investigation aimed at examining the causes of growth and development disorders, while also evaluating the real-world safety and effectiveness of rhGH therapy over the long term (15). IGHD was characterized by a peak GH value below 10 ng/mL following two different GH stimulation tests, low levels of insulin-like growth factor 1 (IGF-1), delayed bone age, no other pituitary hormone abnormalities and normal pituitary magnetic resonance imaging (MRI).

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Research studies involving human subjects were reviewed and approved by the Ethics Committee of the Affiliated Hospital of Jining Medical University (No. JYFY-2015-019). Prior to their participation in the study, written informed consent was obtained from the legal guardians of the participants.

Clinical and laboratory assessments

Participants' height was assessed using a stadiometer, while weight was measured with an electronic scale. Height was presented as the standard deviation score (SDS) according to the normative values for Chinese children (16). Pubertal development was evaluated through a physical examination based on Tanner staging (17). Patients attended the outpatient clinic for follow-up every 3 months. Adult height was determined as the height attained by the patient at Tanner stage 5 (adult) with a growth velocity lower than 2 cm/year in the preceding year and under 1 cm/year in the past 6 months. IGF-1 serum concentrations were quantified via a chemiluminescence assay conducted on the sophisticated DPC IMMULITE 1000 analyzer manufactured by SIEMENS in Germany. Notably, the assay revealed tight precision with intra-assay and interassay coefficients of variation recorded at 3.0% and 6.2%, respectively. Moreover, the computation of the IGF-1 SDS was based on a meticulous analysis utilizing normative data from demographically matched healthy pediatric cohorts (18).

Statistical analysis

The data is presented in two different formats: either as the mean and standard deviation (SD) or as the median and interquartile range for continuous variables, and in terms of percentages for categorical variables. We employed the χ^2 test for categorical variables, Student's *t*-test for normally distributed data, and the Kruskal-Wallis *H* test for skewed distributions to assess discrepancies between the cohort receiving rhGH and the cohort not receiving rhGH. Furthermore, a simple linear regression analysis was conducted to examine the factors influencing final adult height and the gain in height SDS. Finally, multiple linear regression analyses were performed to ascertain the independent impact of rhGH treatment on final adult height and height SDS gain. The determination of statistical significance was indicated by a two-tailed P value <0.05. The statistical computations were executed utilizing R version 4.2.2, accessible at https://www.R-project.org.

Results

Baseline clinical profiles of the subjects

Information concerning the clinical attributes of all the study participants is detailed in *Table 1*. A comparison was made between the clinical profiles of the 84 patients who received rhGH treatment and the 85 patients who did not receive rhGH treatment at the baseline of the study. Baseline data revealed no significant discrepancies in age (P=0.40), bone age (P=0.36), sex (P=0.22), birth weight (P=0.46), height (P=0.58), height SDS (P=0.93), body weight (P=0.35), body mass index (BMI) (P=0.11), IGF-1 (P=0.94), IGF-1 SDS (P=0.84), and puberty stage (P=0.25) between the two cohorts. Higher birth weights (P=0.01) and lower peak GH levels (P=0.001) were detected in the rhGH-treated group than in the nontreated group.

Improvements in height growth and adult height SDS with rhGH treatment

Table 2 described the comparison of adult height and height improvement in treated and untreated IGHD patients. Following rhGH intervention, the ultimate adult height reached 165.54±7.59 cm in the control group and 169.50±6.93 cm in the treatment group (P=0.006), with a median rhGH treatment duration of 1.55 (0.75–2.83) years. In accordance with the growth standards for Chinese children and adolescents, following rhGH treatment, the final adult height SDS in the treatment group reached −0.45 (−0.94 to 0.05), which was significantly greater than the value of −0.62 (−1.62 to −0.12) in the untreated group (P=0.003) (*Figure 1*). Additionally, the increase in height SDS in the treatment group was 2.10 (1.69 to 2.63), which

Table 1 Baseline characteristics of IGHD patients with and without rhGH treatment

Variables	IGHD (n=169)	Untreated with rhGH (n=85)	Treated with rhGH (n=84)	P
Age (years)	12.80±1.84	12.92±1.86	12.68±1.81	0.40
Bone age (years)	10.93±2.20	11.09±2.21	10.77±2.20	0.36
Sex (male %)	137 (81.07)	72 (84.71)	65 (77.38)	0.22
Birth weight (kg)	3.30±0.48	3.33±0.52	3.27±0.44	0.46
Birth length (cm)	50.41±1.68	49.82±0.55	50.91±2.11	0.01
Height (cm)	139.22±10.35	139.66±10.03	138.78±10.70	0.58
Height SDS	−2.63±0.58	−2.64±0.47	−2.63±0.62	0.93
Body weight (kg)	36.95±10.01	36.23±9.27	37.68±10.71	0.35
BMI (kg/m^2)	18.81±3.63	18.36±3.59	19.26±3.64	0.11
IGF-1 (ng/mL)	211.50 (145.00–311.00)	234.82±119.79	233.37±121.23	0.94
IGF-1 SDS	−1.02 (−1.84 to −0.01)	−0.97±1.38	−1.01±1.46	0.84
Peak GH (ng/mL)	5.10 (3.15–7.18)	5.75±2.73	4.47±2.42	0.001
Pubertal stage				0.25
In prepuberty	92 (54.44)	50 (58.82)	42 (50.00)	
In puberty	77 (45.56)	35 (41.18)	42 (50.00)	

Continuous variables are presented as the mean ± standard deviation or median (interquartile range). Categorical variables are displayed as number (percentage). P<0.05 is considered to be statistically significant. BMI, body mass index; IGF-1, insulin like growth factor-1; GH, growth hormone; IGHD, idiopathic growth hormone deficiency; rhGH, recombinant human growth hormone; SDS, standard deviation score.

Table 2 Comparison of adult height and height improvement in rhGH-treated and untreated IGHD patients

Variables	Treated with rhGH (n=84)	Untreated with rhGH (n=85)	P
Age (years)	18.26±1.43	19.43±2.13	<0.001
Adult height (cm)	169.50±6.93	165.54±7.59	0.006
Adult height SDS	−0.45 (−0.94 to 0.05)	−0.62 (−1.62 to −0.12)	0.003
Follow up duration (years)	5.23 (4.29–6.55)	5.27 (4.57–8.29)	0.32
Treatment duration (years)	1.55 (0.75–2.83)	–	–
Height SDS gain	2.10 (1.69–2.63)	1.76 (0.97–2.59)	0.01

Continuous variables are presented as the mean ± standard deviation or median (interquartile range). P<0.05 is considered to be statistically significant. IGHD, idiopathic growth hormone deficiency; rhGH, recombinant human growth hormone; SDS, standard deviation score.

was significantly greater than the increase of 1.76 (0.97 to 2.59) reported in the untreated group (P=0.01) (*Figure 1*). We further conducted a subgroup analysis by sex. The results remained consistent in both the male and female populations as well as in the total population (Tables S1,S2).

Table 3 shows the improvement in pretreatment height and adult height SDS in patients with IGHD. In the group treated with rhGH, the height SDS before rhGH treatment and the adult height SDS were −2.63±0.62 and −0.45 (−0.94 to 0.05) respectively. The improvement in adult height SDS was significant (P<0.001) (*Figure 2*). In the group not treated with rhGH, the height SDS before rhGH treatment

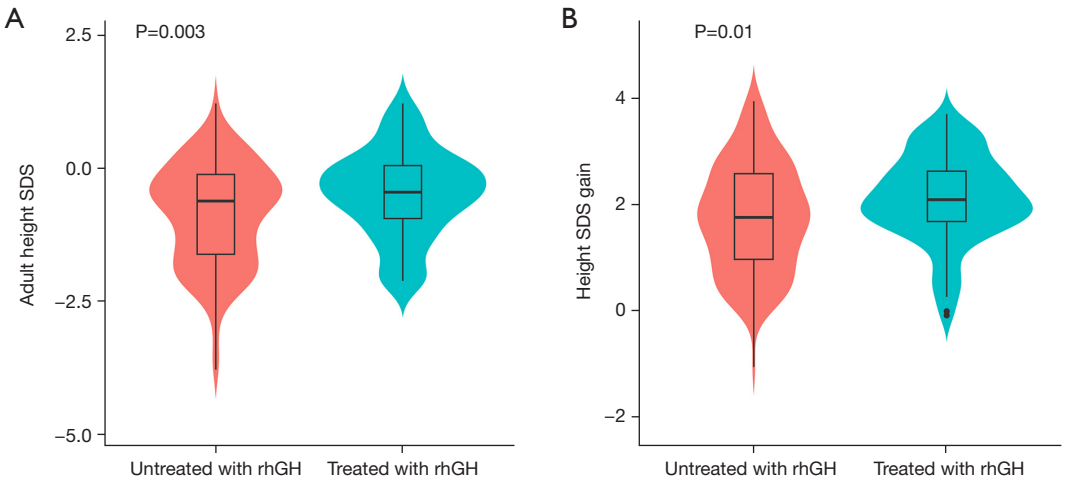

Figure 1 Comparison of adult height and height improvement in rhGH treated and untreated IGHD patients. (A) Adult height SDS; (B) height SDS gain. IGHD, idiopathic growth hormone deficiency; rhGH, recombinant human growth hormone; SDS, standard deviation score.

Table 3 Comparison of height SDS before rhGH treatment and adult height SDS in patients with IGHD

Group	Before rhGH treatment	Follow-up in adulthood	P
Treated with rhGH (N=84)			
Age (years)	12.68±1.81	18.26±1.43	<0.001
Height (cm)	138.78±10.70	167.07±6.93	<0.001
Height SDS	−2.63±0.62	−0.45 (−0.94 to 0.05)	<0.001
Untreated with rhGH (N=85)			
Age (years)	12.92±1.86	19.43±2.13	<0.001
Height (cm)	139.66±10.03	165.54±7.59	<0.001
Height SDS	−2.64±0.47	−0.62 (−1.62 to −0.12)	<0.001

Continuous variables are presented as the mean ± standard deviation or median (interquartile range). P<0.05 is considered to be statistically significant. IGHD, idiopathic growth hormone deficiency; rhGH, recombinant human growth hormone; SDS, standard deviation score.

and the adult height SDS were −2.64±0.47 and −0.62 (−1.62 to −0.12) respectively. The improvement in adult height SDS was also significant (P<0.001) (*Figure 2*).

Variables influencing the growth outcome

We analysed the factors affecting the growth outcome for IGHD patients, the results of which are shown in *Figure 3*. In the patients with IGHD, baseline age (P=0.006), height SDS (P=0.01), and rhGH treatment (P=0.01) significantly affected height SDS gain. However, sex (P=0.85), birth length (P=0.41), birth weight (P=0.41), BMI (P=0.40), IGF-1SDS (P=0.84), peak GH (P=0.30) or duration of rhGH treatment (P=0.29) had no correlation with height SDS gain. Regarding the final adult height SDS, baseline age (P=0.03), bone age (P=0.045), body weight (P=0.003), height SDS (P=0.004), puberty stage (P=0.03) and rhGH treatment (P=0.003) were significantly correlated. In contrast, sex (P=0.87), birth length (P=0.46), birth weight (P=0.33), BMI (P=0.38), IGF-1SDS (P=0.35), peak GH

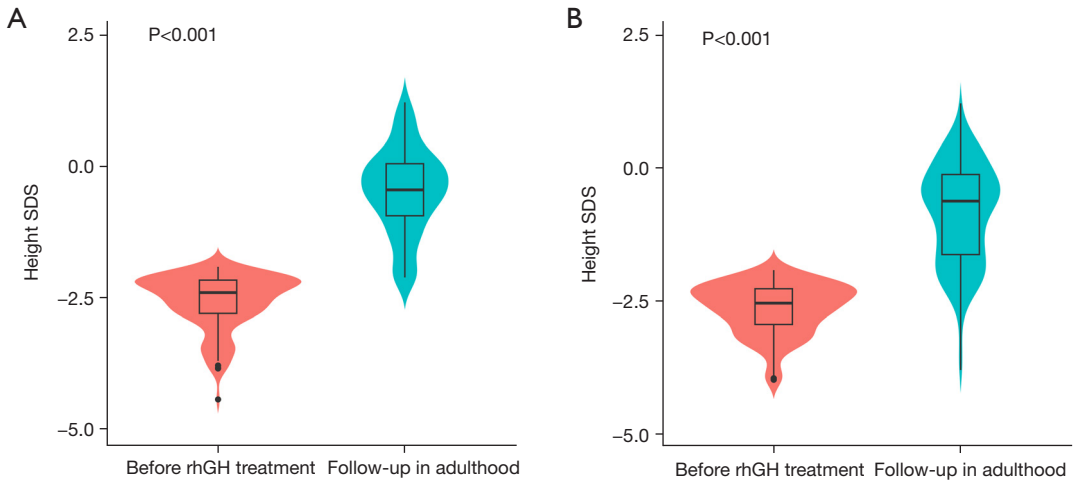

Figure 2 Comparison of height SDS before rhGH treatment and adult height SDS in patients with IGHD. (A) Treated with rhGH; (B) untreated with rhGH. IGHD, idiopathic growth hormone deficiency; rhGH, recombinant human growth hormone; SDS, standard deviation score.

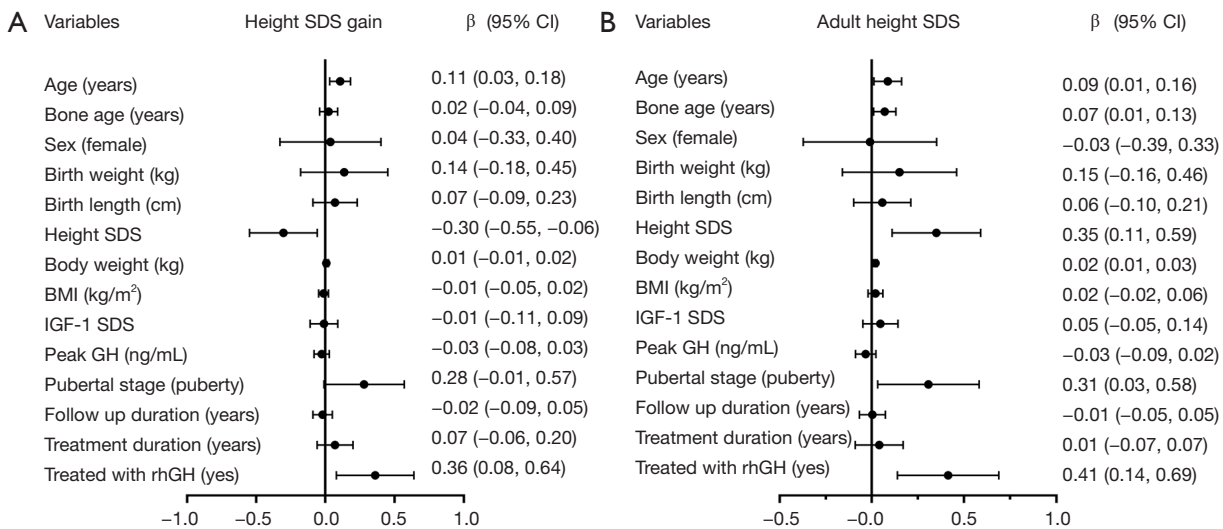

Figure 3 Associations between growth outcomes and clinical characteristics in patients with IGHD. (A) Height SDS gain; (B) final adult height SDS. BMI, body mass index; CI, confidence interval; IGF-1, insulin like growth factor-1; IGHD, idiopathic growth hormone deficiency; rhGH, recombinant human growth hormone; SDS, standard deviation score.

(P=0.20) or duration of rhGH treatment (P=0.57) showed no correlation with the increase in final adult height.

Multiple regression analysis of predictors of growth outcome

Multiple regression analysis was conducted following adjustments for potential confounding variables identified in the univariate analysis, such as age, gender, birth weight, birth length, height, and peak GH levels. This was done to explore the independent correlation between rhGH treatment and the attainment of final adult height as well as height SDS improvement. There was a positive association between rhGH treatment and height SDS gain [β=0.40, 95% confidence interval (CI): 0.11, 0.68; P=0.007]. Furthermore, compared with that of patients not receiving rhGH treatment, the adult height SDS of patients receiving

rhGH treatment was significantly greater (β=0.41, 95% CI: 0.14, 0.69; P=0.003) (Table S3).

Discussion

In this study, we conducted a clinical observational investigation to evaluate the impact of rhGH on linear growth and final adult height in children with IGHD. Our findings suggest that rhGH therapy had a positive impact on height development, leading to a significant improvement in the adult height SDS among patients treated with rhGH compared to those without rhGH treatment.

GH is essential for normal growth, cell reproduction, and regeneration. In patients with IGHD, the lack of endogenous GH leads to growth retardation. The administration of rhGH effectively compensates for this deficiency, promoting linear growth during the growth spurt periods and ultimately increasing adult height (19). The effectiveness of rhGH replacement therapy in enhancing height growth during childhood and ultimately adult height is widely recognized (20). In a recent study, 123 patients with GHD were monitored until they reached their final adult height following rhGH therapy. The findings indicated that the final adult height in GHD patients was −1.84±0.89 (21). In our investigation, however, the final adult height among GHD patients was elevated by −0.45 (−1.28 to −0.02) in comparison. This may be due to the greater baseline height of −2.63±0.58 in our study than that of −3.65±1.07 in the previous study (20). Reiter *et al.* analysed 1,258 children with IGHD based on the basis of data from the International Growth Database (KIGS), and concluded that rhGH treatment can significantly improve the height of IGHD patients, increasing the near-adult height (NAH) of most patients close to their genetic potential, emphasizing the importance of early intervention and long-term treatment (22). Polak *et al.*, basis of the NordiNet® International Outcome Study, analysed 172 IGHD children who reached NAH, and reported 78.5% of the patients achieved a normal NAH (>−2 SDS), providing important evidence for the effectiveness of rhGH treatment in IGHD patients (23). Furthermore, a large-scale cohort study on rhGH replacement therapy in children revealed that the average increase in height approaching adulthood was approximately 2 SDS of the baseline height (23). The results of this study are consistent with these findings and further confirm the effectiveness of rhGH treatment in Chinese patients with IGHD. These results will help guide clinical treatment decisions for children with IGHD in China.

The improvements in growth and adult height observed in treated patients can be attributed to several mechanisms. Firstly, rhGH stimulates the liver and other tissues to produce IGF-1 (24). IGF-1 is a key mediator of the growth-promoting effects of GH. It acts on chondrocytes in the growth plates of long bones, promoting their proliferation and differentiation, which in turn leads to bone growth (25). Secondly, rhGH has anabolic effects on muscle and other tissues. It increases protein synthesis, enhances nitrogen retention, and promotes lipolysis. These metabolic changes contribute to overall growth and development (26-28). Additionally, rhGH may also have direct effects on the growth plates independent of IGF-1, although the exact nature of these effects is still an area of active research (29).

Multiple variables have been identified to impact the response of short-statured children to rhGH therapy. Predictably, these factors have a dual influence on both the ultimate adult height and the effectiveness of rhGH in children with short stature. Previous studies have shown that the growth response to rhGH in patients of short stature was associated with height and height SDS at the start of treatment, age at the start of treatment, stage of puberty, duration of treatment, rhGH dose, midparental height (MPH) or target height, and delayed bone age (30,31). In the present study, the initial height SDS was linked to the eventual adult height of individuals with IGHD. These findings underscore the importance of considering rhGH therapy for patients with IGHD, as their natural growth trajectory may be compromised into adulthood. In fact, for patients clinically diagnosed with IGHD who face no tumor-related risks, we advocate for rhGH treatment across the board. Nevertheless, in China, rhGH treatment was previously entirely self-funded and not covered by medical insurance. Additionally, the expense of rhGH treatment is extremely high, and the treatment period is prolonged. As a result, numerous families voluntarily opted not to pursue the treatment because they were unable to shoulder the financial burden.

The strengths of this study are that it analysed the final adult height achieved by children with IGHD, and also incorporated of children who experienced normal growth without rhGH intervention. This long-term perspective provides real-world evidence on how rhGH treatment impacts the ultimate height outcome of patients. There are several limitations to this study. Firstly, this study had a retrospective design and lacked randomization, which may have led to selection bias. Future randomized controlled

trials are needed to further validate the effects of rhGH treatment in patients with IGHD. Secondly, as this study involved a retrospective study design, there may have been confounding indications in which the underlying reason for starting rhGH treatment may have also been related to the final adult height. However, no significant differences in baseline clinical characteristics, including age, sex, height, height SDS, stage of puberty, or cause of short stature, were found between the rhGH-treated group and the rhGH-untreated group. Nevertheless, the possibility that there are residual confounding factors in play cannot be avoided completely, and the described associations should be viewed in this light rather than as evidence of causality. Finally, the height of most patients with short stature improves their height in adulthood; therefore, the examination of the laboratory indicators in these patients is limited, and the laboratory data from patients in adulthood are missing in this study.

Conclusions

In conclusion, our study shows that treatment with rhGH increases final adult height and height gain in patients with IGHD. After rhGH treatment, the adult height of most patients reached the height range of patients in the normal population. The adult height of IGHD patients without rhGH treatment is impaired, and the application of rhGH treatment is necessary for children with IGHD.

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None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-2024-576/rc

Data Sharing Statement: Available at https://tp.amegroups.com/article/view/10.21037/tp-2024-576/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-2024-576/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Research studies involving human subjects were reviewed and approved by the Ethics Committee of the Affiliated Hospital of Jining Medical University (No. JYFY-2015-019). Prior to their participation in the study, written informed consent was obtained from the legal guardians of the participants.

References

1. Tidblad A. The history, physiology and treatment safety of growth hormone. Acta Paediatr 2022;111:215-24.
2. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. GH Research Society. J Clin Endocrinol Metab 2000;85:3990-3.
3. Binder G, Schnabel D, Reinehr T, et al. Evolving pituitary hormone deficits in primarily isolated GHD: a review and experts' consensus. Mol Cell Pediatr 2020;7:16.
4. Voss LD, Sandberg DE. The psychological burden of short stature: evidence against. Eur J Endocrinol 2004;151 Suppl 1:S29-33.

5. Noeker M. Psychological functioning in idiopathic short stature. Horm Res Paediatr 2011;76 Suppl 3:52-6.
6. Tanaka T, Tai S, Morisaki Y, et al. Evaluation of Quality of Life in Children with GH Deficiency and Idiopathic Short Stature Using the Child Behavior Checklist. Clin Pediatr Endocrinol 2009;18:15-22.
7. Bullinger M, Bloemeke J, Mericq V, et al. Quality of Life in Adolescent Boys with Idiopathic Short Stature: Positive Impact of Growth Hormone and Aromatase Inhibitors. Horm Res Paediatr 2018;90:381-92.
8. Bloemeke J, Balacano Valdez R, Mauras N, et al. Psychometric performance of the Quality of Life in Short Stature Youth (QoLISSY) questionnaire in a randomized open-label comparator trial in idiopathic short stature. J Pediatr Endocrinol Metab 2019;32:1089-101.
9. Richmond E, Rogol AD. Treatment of growth hormone deficiency in children, adolescents and at the transitional age. Best Pract Res Clin Endocrinol Metab 2016;30:749-55.
10. Collett-Solberg PF, Ambler G, Backeljauw PF, et al. Diagnosis, Genetics, and Therapy of Short Stature in Children: A Growth Hormone Research Society International Perspective. Horm Res Paediatr 2019;92:1-14.
11. Ranke MB, Wit JM. Growth hormone - past, present and future. Nat Rev Endocrinol 2018;14:285-300.
12. Maghnie M, Ranke MB, Geffner ME, et al. Safety and Efficacy of Pediatric Growth Hormone Therapy: Results From the Full KIGS Cohort. J Clin Endocrinol Metab 2022;107:3287-301.
13. Chae HW, Hwang IT, Lee JE, et al. Height outcomes in Korean children with idiopathic short stature receiving growth hormone treatment. Front Endocrinol (Lausanne) 2022;13:925102.
14. Al Alwan I, Alfaraidi H, Al Juraibah F, et al. Timing of Puberty and Late Pubertal Height in Saudi Schoolboys: Riyadh Puberty Study II. Int J Endocrinol 2022;2022:4343596.
15. Zhao Q, Zhang M, Chu Y, et al. A Retrospective Analysis of Patients with Short Stature in Eastern China between 2013 and 2019. Biomed Res Int 2021;2021:6640026.
16. Li H, Ji CY, Zong XN, et al. Height and weight standardized growth charts for Chinese children and adolescents aged 0 to 18 years. Chinese J Pediatr 2009;47:487-92.
17. Wright CM, Ahmed L, Dunger DB, et al. Can we characterise growth in puberty more accurately? Validation of a new Puberty Phase Specific (PPS) growth chart. Arch Dis Child 2012;97:A100.
18. Isojima T, Shimatsu A, Yokoya S, et al. Standardized centile curves and reference intervals of serum insulin-like growth factor-I (IGF-I) levels in a normal Japanese population using the LMS method. Endocr J 2012;59:771-80.
19. Tidblad A, Sävendahl L. Childhood growth hormone treatment: challenges, opportunities, and considerations. Lancet Child Adolesc Health 2024;8:600-10.
20. Ranke MB. Short and Long-Term Effects of Growth Hormone in Children and Adolescents With GH Deficiency. Front Endocrinol (Lausanne) 2021;12:720419.
21. Demiral M, Unal E, Baysal B, et al. Evaluation of the Final Adult Height and Its Determinants in Patients with Growth Hormone Deficiency: A Single-centre Experience from the South-Eastern Region of Turkey. J Clin Res Pediatr Endocrinol 2020;12:295-302.
22. Reiter EO, Price DA, Wilton P, et al. Effect of growth hormone (GH) treatment on the near-final height of 1258 patients with idiopathic GH deficiency: analysis of a large international database. J Clin Endocrinol Metab 2006;91:2047-54.
23. Polak M, Blair J, Kotnik P, et al. Early growth hormone treatment start in childhood growth hormone deficiency improves near adult height: analysis from NordiNet® International Outcome Study. Eur J Endocrinol 2017;177:421-9.
24. Kaplan SA, Cohen P. The somatomedin hypothesis 2007: 50 years later. J Clin Endocrinol Metab 2007;92:4529-35.
25. Yakar S, Werner H, Rosen CJ. Insulin-like growth factors: actions on the skeleton. J Mol Endocrinol 2018;61:T115-37.
26. Vijayakumar A, Yakar S, Leroith D. The intricate role of growth hormone in metabolism. Front Endocrinol (Lausanne) 2011;2:32.
27. Vijayakumar A, Novosyadlyy R, Wu Y, et al. Biological effects of growth hormone on carbohydrate and lipid metabolism. Growth Horm IGF Res 2010;20:1-7.
28. Moller N, Vendelbo MH, Kampmann U, et al. Growth hormone and protein metabolism. Clin Nutr 2009;28:597-603.
29. Baron J, Sävendahl L, De Luca F, et al. Short and tall stature: a new paradigm emerges. Nat Rev Endocrinol 2015;11:735-46.
30. Paltoglou G, Dimitropoulos I, Kourlaba G, et al. The effect of treatment with recombinant human growth hormone (rhGH) on linear growth and adult height in children with idiopathic short stature (ISS): a systematic review and meta-analysis. J Pediatr Endocrinol Metab

2020;33:1577-88.
31. Soliman AT, Elawwa A, Itani M, et al. Responses to growth hormone (GH) therapy in short children with normal GH secretion and no bone age delay: an analysis of potential factors affecting their response to rhGH therapy. A controlled study. Acta Biomed 2019;90:43-51.

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