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Real-world Clinical Study of Recombinant Human Growth Hormone in the Treatment of Idiopathic Short Stature

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Abstract: *Objective:* To investigate the clinical efficacy and safety evaluation of Polyethylene Glycol Recombinant Human Growth Hormone Injection (PEG-rhGH) in the treatment of idiopathic short stature. *Methods:* A total of 1402 patients were enrolled from March 21, 2024 to January 13, 2025, including 778 males and 624 females, with ages mainly ranging from 5 to 13 years old. Follow-up visits were completed by 488 patients for the first time, 174 patients for the second time, and 81 patients for the third time. All patients were treated with PEG-rhGH (Jin Sai Zeng) as the main therapy after admission. The changes in height information, IGF-1, and thyroid examination results of each patient at the initial diagnosis, 6, 9, and 12 months after treatment were observed and analyzed. *Results:* There was no statistical difference between the baseline and the initial diagnosis, as well as the second follow-up visit ($P < 0.05$), while there was a statistical difference between the baseline and the first and third follow-up visits ($P > 0.05$). There was a statistically significant difference in IGF-1 between the initial diagnosis and the first follow-up visit ($P < 0.05$), but no statistical difference between the first, second, and third follow-up visits ($P > 0.05$). Additionally, IGF-1 levels increased with time. There was no statistical difference in TSH between the initial diagnosis and the first, second, and third follow-up visits ($P > 0.05$). There was a statistical difference in free T3 between the initial diagnosis and the first and second follow-up visits ($P < 0.05$), but no statistical difference between the second and third follow-up visits ($P > 0.05$). There was no statistical difference in free T4 between the initial diagnosis and the first and second follow-up visits ($P > 0.05$), but there was a statistical difference between the second and third follow-up visits ($P < 0.05$). *Conclusion:* PEG-rhGH (Jin Sai Zeng) is significantly effective in improving height and IGF-1 levels in patients with idiopathic short stature.

Keywords: Recombinant human growth hormone; Idiopathic short stature; Clinical efficacy

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1. Introduction

Idiopathic short stature (ISS) refers to an abnormal growth and development condition characterized by

unexplained growth retardation or stagnation at a relatively low level. It is currently believed to be associated with genetic and environmental factors, with an incidence rate of 1% to 3%. The clinical manifestations include short stature, often accompanied by symptoms such as delayed bone age and undeveloped secondary sexual characteristics. Approximately 60% to 80% of children with short stature have ISS, which affects their physical development and self-confidence. If not corrected promptly, it can have severe adverse effects on their lives. A study of 136 children with short stature in Changde, Hunan Province, found that there were more boys than girls, with an average age of 11.2 years, and 38 children (27.94%) had ISS [1]. Another study of 5613 children in Shantou, Guangdong Province, found that 127 children had short stature, with a prevalence rate of 2.26%, mainly in the age range of 3 to 16 years old, and 38 children (29.92%) had ISS [2]. Recombinant human growth hormone is a peptide hormone that mainly acts on the growth plate of bones, promoting cell division and proliferation in bone tissue, and stimulating continuous proliferation of epiphyseal chondrocytes to increase the patient's height [3]. Additionally, from a pharmacoeconomic perspective, the cost of treatment is lower than that of pharmacological therapy but still higher than what ordinary families can afford [4]. This study aims to retrospectively investigate the clinical data of patients with idiopathic short stature treated in our hospital from July 1 to September 30, 2024, and to explore the impact of factors such as disease severity and bone age delay on the effectiveness of recombinant human growth hormone treatment for IA. The goal is to provide a reference for the rational use of growth hormone in clinical practice and theoretical support for the development of relevant intervention measures. (Note: There are some inconsistencies in the time periods mentioned in the abstract, which may need to be revised for clarity and accuracy.)

2. Materials and methods

2.1. General information

From March 21, 2024, to January 13, 2025, a total of 1402 individuals were enrolled, including 778 males and 624 females. The patients' ages were mainly between 5 and 13 years old. Subsequently, 488 people completed the first follow-up, 174 completed the second follow-up, and 81 completed the third follow-up. The enrolled patients were mainly from departments such as Child Health Care, Pediatric Endocrinology, Pediatric Respiratory, and Endocrinology.

Inclusion Criteria: (1) Pre-pubescent children (aged 3 to 14 years), gender unrestricted; (2) Symmetrical short stature, with height falling behind the 3rd percentile (P3, -1.88SD) or 2 standard deviations (SD) of the growth curve for normal children of the same age and gender; (3) Any drug provocation test result indicating a GH peak value >10ug/l; (4) Slow growth, with a growth rate of < 5cm/year; (5) Normal intelligence, mental state, and consciousness; (6) Normal birth length, weight, and body proportions, with no evidence of systemic, endocrine, nutritional, chromosomal abnormalities, or genetic variations; (7) After full communication, the patients' families are informed and agree to treatment with polyethylene glycol recombinant human growth hormone injection (Jinsai Zeng) and have signed an informed consent form.

Exclusion Criteria: (1) Exclusion of other primary (e.g., genetic syndromes) and secondary growth disorders that affect growth, including various diseases related to the environment, hormones, nutrition, and/or systemic organic diseases, such as Cushing's syndrome, hypothyroidism, pseudohypoparathyroidism, growth hormone deficiency, bone/cartilage disease, small for gestational age, chromosomal diseases, Turner syndrome, Noonan syndrome, etc.; (2) Allergy to polyethylene glycol recombinant human growth hormone injection (Jinsai Zeng) and its excipients; (3) Presence of diseases and tumors unsuitable for growth hormone therapy, such as cardiac, liver, kidney, and other

important organ dysfunctions and other chronic diseases, or pituitary dysfunction, cerebrovascular disease, etc.; (4) Other situations where the researcher believes it is not appropriate to adopt growth hormone therapy.

2.2. Methods

All patients were treated primarily with polyethylene glycol recombinant human growth hormone injection (Jinsai Zeng) after admission. For some children with a shorter duration of illness and a lesser degree of disease, oral medication and physical therapy were used in addition to rhGH. For children with complex conditions and multiple comorbidities, rhGH was used alone.

2.3. Observation indicators

The changes in height information, IGF-1, and thyroid test results of each patient were observed at the initial diagnosis and after 6, 9, and 12 months of treatment.

2.4. Statistical methods

SPSS 27.0 statistical software was used for statistical analysis of the data. Measurement data were expressed as mean ± standard deviation, and the t-test was used for comparison between groups. Count data were expressed as a percentage (%), and the $\chi 2$ test was used for comparison between groups.

3. Results

3.1. Changes in height information

There was no statistical difference between the baseline and the initial diagnosis, as well as the second follow-up ($P < 0.05$). However, there was a statistical difference between the baseline and the first and third follow-ups ($P > 0.05$). See Table 1 for details.

Table 1. Height information (, cm)

Group	Number of Cases	Height Information
Baseline	1402	123.50 ± 17.78
Initial diagnosis	1402	125.58 ± 49.43
The first follow-up	488	128.05 ± 52.15
The second follow-up	174	125.41 ± 15.49
The third follow-up	81	128.12 ± 14.44
t		1.483[a] 2.830[b] 1.355[c] 2.295[d]
P		> 0.05[a] 0.005[b] > 0.05[c] 0.022[d]

Note: a, b, c, and d represents the comparison between baseline and initial diagnosis, first follow-up, second follow-up, and third follow-up, respectively.

3.2. Patient IGF-1

There was a statistically significant difference in IGF-1 levels between the initial diagnosis and the first follow-up ($P < 0.05$). However, there were no statistically significant differences between the first, second, and third follow-ups when compared pairwise ($P > 0.05$). Additionally, IGF-1 levels increased with time, as shown in **Table 2**.

Table 2. Patient IGF-1 (U/mL)

Group	Number of Cases	IGF-1
Baseline	1402	186.22 ± 120.95
Initial diagnosis	488	268.51 ± 128.24
The first follow-up	174	275.24 ± 116.70
The second follow-up	81	304.02 ± 114.43
The third follow-up		12.742[a] 0.608[b] 1.845[c]
P		0.000[a] > 0.05[b] > 0.05[c]

Note: a, b, and c represent the comparison between the first follow-up and initial diagnosis, the first follow-up and second follow-up, and the second follow-up and third follow-up, respectively. The actual table with data would follow this text in a formatted document.

3.3. Thyroid test results

There were no statistically significant differences in TSH levels between the initial diagnosis and any of the follow-ups (first, second, and third) when compared pairwise ($P > 0.05$). For free T3, there were statistically significant differences between the initial diagnosis and both the first and second follow-ups ($P < 0.05$), but no difference between the second and third follow-ups ($P > 0.05$). For free T4, there were no statistically significant differences between the initial diagnosis and the first or second follow-ups ($P > 0.05$), but there was a difference between the second and third follow-ups ($P < 0.05$). See **Table 3** for details.

Table 3. Thyroid test results (μIU/mL)

Group	Number of Cases	TSH	Free T3	Free T4
Baseline	1402	2.95 ± 8.25	5.43 ± 1.53	13.36 ± 13.67
Initial diagnosis	488	2.48 ± 1.37a	5.46 ± 1.48a	47.89 ± 771.67a
The first follow-up	174	2.45 ± 1.10b	5.98 ± 1.32b	15.47 ± 5.22b
The second follow-up	81	2.18 ± 0.87c	5.95 ± 1.19c	17.63 ± 2.90c
The third follow-up		1.252[a] 0.260[b] 1.944[c]	12.916[a] 4.090[b] 0.174[c]	1.676[a] 0.554[b] 3.480[c]
P		> 0.05[a] > 0.05[b] > 0.05[c]	0.000[a] 0.000[b] > 0.05[c]	> 0.05[a] > 0.05[b] 0.001[c]

Note: a, b, and c represents the comparison between the first follow-up and initial diagnosis, the first follow-up and second follow-up, and the second follow-up and third follow-up, respectively.

4. Discussion

Idiopathic short stature (ISS) refers to a group of heterogeneous short stature diseases with unknown etiology. It refers to children whose height is below 2 standard deviations (SD) of the mean height for their age, gender, and ethnicity, or below the 3rd percentile (P3, -1.88 SD), and whose birth length, weight, and body proportions are normal without evidence of systemic, endocrine, nutritional, chromosomal abnormalities, or genetic variations [5]. The etiology of ISS is complex, and its occurrence is closely related to growth hormone secretion disorders or deficiencies, growth hormone resistance, and insufficient activity [6–8]. Therefore, recombinant human growth hormone (rhGH) therapy is one of the main treatments for children with ISS. In 2021, the China National Medical Products Administration approved rhGH for the treatment of ISS and suggested adjusting treatment based on growth response, i.e., the rate of height increase. Ling *et al.* interpreted the guidelines and proposed that due to the high heterogeneity of ISS patients, their physical and psychological factors, dosage, treatment risks, and benefits should be more carefully evaluated during growth hormone therapy [9,10].

Jinseiseng is the first long-acting growth hormone independently developed in China and the world's first polyethylene glycolated growth hormone injection to be listed. The successful launch of the long-acting growth hormone brand has reduced the injection frequency from once a day to once a week, ending the history of needing daily growth hormone injections for treatment. Compared to short-acting growth hormone, the long-acting formulation has a longer duration of action. The main reason is that the long-acting growth hormone utilizes a natural peptide bond to connect inert PEG and naturally structured growth hormone, much like putting a huge armor on the growth hormone. This significantly reduces the speed of its filtration by the kidneys, decreases protease degradation, and enhances the stability of the growth hormone drug in the human body [11, 12]. Therefore, the elimination rate of the drug is greatly slowed down, and the duration of the drug effect is significantly increased.

The results of this study showed that analyzing the height SDS data of patients who completed three follow-ups indicated a relatively positive treatment effect during the treatment phase. Most patients showed significant initial treatment effects and had relatively stable efficacy. There was no statistically significant difference between the baseline and the first and second follow-ups ($P < 0.05$), but there was a statistically significant difference between the baseline and the first and third follow-ups ($P > 0.05$). These results suggest that there are statistically significant differences in height SDS values at different follow-up time points, and these values improve with time.

Statistical analysis of patients' IGF-1 showed an increasing trend in insulin-like growth factor-1. The t-test revealed a statistically significant difference between groups, with IGF-1 levels increasing over time.

Statistical analysis was conducted on patients' TSH (Thyroid Stimulating Hormone), free T3 (free triiodothyronine), and free T4 (free thyroxine levels). The t-test results showed no statistically significant differences, indicating that the treatment had no significant effect on patients' thyroid function. These results suggest that there are statistically significant differences in height SDS values at different follow-up time points, and these values improve with time. Statistical analysis of patients' IGF-1 showed an increasing trend, and the t-test revealed a statistically significant difference between groups. Both the first and second follow-ups showed statistically significant differences compared to the baseline. Moreover, the treatment had no significant effect on the patients' thyroid function.

5. Conclusion

In summary, recombinant human growth hormone (Jinsaizeng) treatment for idiopathic short stature has significant efficacy in improving patients' height and IGF-1 levels. This study provides strong clinical evidence

for the application of rhGH in the treatment of idiopathic short stature. Future studies can further validate the long-term effects and economic value of rhGH treatment by extending follow-up time, expanding sample size, and optimizing stratified analysis, providing more comprehensive guidance for clinical practice.

Disclosure statement

The authors declare no conflict of interest.

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