



The effects of growth hormone treatment on height in short children

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Growth hormone therapy was introduced in 1958 when growth hormone extracted from the pituitary gland was first used for growth hormone deficiency (GHD) patients. However, its use was discontinued in 1985 after it was found to be associated with Creutzfeldt-Jakob disease.¹⁾ After that, recombinant human growth hormone (rhGH) therapy, available since 1985, was approved not only for growth disturbances linked to GHD, but also for short stature associated with other conditions, such as Turner syndrome, Noonan syndrome, Prader-Willi syndrome, short stature homeobox-containing gene deficiency, chronic renal insufficiency and idiopathic short stature (ISS), as well as in children who are small for gestational age (SGA).²⁾

Experience gained during the last 15–20 years has shown that GH treatment is effective in restoring normal growth in children with GHD and other forms of growth retardation, including ISS and SGA with insufficient catch-up growth. Meta-analysis of results from 21 clinical studies indicated that children with ISS who received rhGH had significantly higher height increment at the end of the first year than the control group, an effect that persisted in the second year of treatment. This treatment also improved final adult height. The difference between the 2 groups was equal to 5.3 cm for male patients and 4.7 cm for female patients.³⁾ Results from subjects in a large observational study in Korea demonstrated increased height standard deviation score (SDS) from the baseline in subjects with GHD and ISS.⁴⁾

Yoon et al.⁵⁾ evaluated growth response to GH treatment for 2 years in patients with GHD and ISS. In addition, the authors sought to evaluate whether there was a difference in the effect of GH therapy according to peak GH on GH stimulation test. They reported no difference in height SDS and height velocity between GHD and ISS patients after treatment with growth hormone for 2 years. Moreover, there was no significant difference in the response to growth hormone treatment according to peak GH among GHD patients.

This result may be due to reduced sensitivity and specificity of the GH stimulation test. The reliability of pharmacological tests used for GH secretion evaluation has been repeatedly questioned given the lack of normal age-related reference values, the use of different pharmacological stimuli and different laboratory methods for the measurement of circulating GH.⁶⁾ Lee and Hwang⁷⁾ reported that when 48 patients with ISS underwent repeat GH stimulation test, 9 (18.7%) were diagnosed with GH deficiency (peak GH < 10 ng/mL). The validity of GH measurements as the arbitrary gold standard for the diagnosis of GHD is questionable and alternative or complementary approaches should be developed, including insulin-like growth factor-1 and auxological parameters.

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See the article "Response to growth hormone according to provocation test results in idiopathic short stature and idiopathic growth hormone deficiency" via <https://doi.org/10.6065/apem.2142110.055>.

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References

1. Preece MA. Creutzfeldt-Jakob disease: implications for growth hormone deficient children. *Neuropathol Appl Neurobiol* 1986;12:509-15.
2. Savage MO, Storr HL. Balanced assessment of growth disorders using clinical, endocrinological, and genetic approaches. *Ann Pediatr Endocrinol Metab* 2021;26:218-26.
3. Paltoglou G, Dimitropoulos I, Kourlaba G, Charmandari E. 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.
4. Rhie YJ, Yoo JH, Choi JH, Chae HW, Kim JH, Chung S, et al. Long-term safety and effectiveness of growth hormone therapy in Korean children with growth disorders: 5-year results of LG Growth Study. *PLoS One* 2019;14:e0216927.
 5. Yoon JY, Cheon CK, Lee JH, Kwak MJ, Kim HJ, Kim YJ, et al. Response to growth hormone according to provocation test results in idiopathic short stature and idiopathic growth hormone deficiency. *Ann Pediatr Endocrinol Metab* 2022;27:37-43.
 6. Hilczer M, Smyczynska J, Lewinski A. Limitations of clinical utility of growth hormone stimulating tests in diagnosing children with short stature. *Endocr Regul* 2006;40:69-75.
 7. Lee HS, Hwang JS. Influence of body mass index on growth hormone responses to classic provocative tests in children with short stature. *Neuroendocrinology* 2011;93:259-64.