

Efficacy And Safety Of Long-Term Continuous Growth Hormone Treatment In Children With Prader-Willi Syndrome

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Patients with PWS have an abnormal body composition with increased fat mass and decreased lean body mass, and short stature. Some studies showed normalization of adult height when GH treatment was started before onset of puberty. Although improvement of body composition is considered the most important effect of GH in children with PWS, there are no reports regarding effects of long-term GH treatment on body composition in a large group of patients. We investigated long-term efficacy and safety of GH treatment on body composition, growth, bone maturation, and safety parameters, in 55 children with PWS included in a 4-year national multicenter prospective follow-up study. The mean \pm SD age at start of study was 5.9 ± 3.2 years. All children received somatropin $1 \text{ mg/m}^2\text{-day}$. The following data were annually obtained in one center: fat% and lean body mass (LBM) by dual-energy x-ray absorptiometry, height, weight, head circumference, bone age, blood pressure, and fasting IGF-I, IGFBP-3, glucose, insulin, HbA1c, total cholesterol, HDL, and LDL. SD-scores were calculated according to Dutch and PWS reference values (SDS and SDS_{PWS}).

Fat%SDS was significantly lower after 4 years of GH treatment ($p < 0.0001$). LBMSDS significantly increased during the first year ($p = 0.02$), but returned to baseline values the second year and remained unchanged thereafter. Thus, LBM stabilized during long-term continuous GH treatment, which is in contrast to the persistent decrease of LBMSDS commonly observed in untreated children with PWS. Mean \pm SD height normalized from -2.27 ± 1.2 SDS to -0.24 ± 1.2 SDS ($p < 0.0001$). Head circumference SDS increased from -0.79 ± 1.0 at start to 0.07 ± 1.1 SDS after 4 years. BMISDS_{PWS} significantly decreased. Mean \pm SD IGF-I and the IGF-I/IGFBP-3 ratio significantly increased to 2.08 ± 1.1 and 2.32 ± 0.9 SDS, respectively. GH treatment had no adverse effects on bone maturation, blood pressure, glucose homeostasis, and serum lipids.

Our study shows that 4 years of continuous GH treatment with a standard dose ($1 \text{ mg/m}^2\text{-day}$) had a significant favorable effect on body composition, heightSDS, BMISDS_{PWS}, and head circumference SDS, without adverse effects on blood pressure, glucose homeostasis, and serum lipids. Importantly, the favorable effect on body composition persisted during the 4 years of study. Based on our findings, it is recommended to keep IGF-I levels between 2 and 3 SDS for optimal effects in children with PWS, without adverse effects. **In conclusion, long-term continuous GH treatment is an effective and safe therapy for children with PWS.**

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