

Two years of replacement therapy in adults with growth hormone deficiency.

Clin Endocrinol (Oxf). 1997 Oct;47(4):485-94.

[Verhelst J](#), [Abs R](#), [Vandeweghe M](#), [Mockel J](#), [Legros JJ](#), [Copinschi G](#), [Mahler C](#), [Velkeniers B](#), [Vanhaelst L](#), [Van Aelst A](#), [De Rijdt D](#), [Stevenaert A](#), [Beckers A](#).

Department of Endocrinology, Algemeen Ziekenhuis Middelheim, Antwerpen, Belgium.

OBJECTIVES: Although several studies have shown beneficial short-term effects of recombinant human growth hormone (rhGH) therapy in adult GH deficient (GHD) patients, few data are available on large groups of patients treated for more than one year. In addition, the optimal dose of rhGH for each patient and the baseline parameters that predict which patients will benefit most from therapy or will have adverse events are not entirely elucidated. **DESIGN:** 148 adult GHD patients were enrolled in a multicentre 2-year rhGH replacement study which was placebo controlled for the first six months. rhGH (Genotropin/Genotonorm Pharmacia & Upjohn) was given in a dose of 0.25 IU/kg/week sc (1.5 IU/m²/day). **MEASUREMENTS:** Every 3-6 months body composition was measured using body impedance analysis and general well being was assessed using the Nottingham Health Profile (NHP) and social self-reporting questionnaire. At the same time patients had a full clinical examination and blood was sampled for glucose, HbA1c, IGF-1, creatinine, full blood count, thyroid hormones and liver function tests. **RESULTS:** With rhGH therapy IGF-1 levels increased from -2.00 +/- 2.60 SDS to 1.47 +/- 2.6 SDS after six months ($P < 0.001$), continued to rise despite no change in dose to 1.84 +/- 2.8 SDS after one year and remained constant thereafter (1.98 +/- 2.4 after 2 years). 56% of patients ultimately attained supranormal IGF-1 levels (+2 SD), 22% had levels below the mean, of which 9% were below -2 SD. Within 3 months lean body mass (LBM) increased by +5.09% ($P < 0.001$), total body water (TBW) by +5.40% ($P < 0.001$), while body fat (BF) dropped by -10.89% ($P < 0.001$) and waist circumference by -1.42% ($P < 0.004$). These effects were maintained during the first year of therapy, but the effect was attenuated after 24 months: LBM, +3.91% ($P < 0.001$); TBW, +3.28%, $P < 0.001$, BF, -6.42% ($P < 0.001$) and waist -2.22% ($P < 0.009$). Individual differences in response were large and could not be predicted by any of the baseline parameters, except for a better response in males. Treatment resulted in a large and progressive improvement on the NHP scale, especially energy, emotions and sleep, but a similar change was also found in patients during placebo treatment. With rhGH the number of full days of sick leave/6 months decreased from 12.17 +/- 3.90 days (SEM) to 7.15 +/- 3.50 days after six months ($P = 0.009$), 2.93 +/- 1.55 days after 12 months ($P = 0.01$), 0.39 +/- 0.17 days after 18 months ($P < 0.001$) and 3.3 +/- 2.51 days after 24 months ($P = 0.026$). Similarly, the hospitalization rate went down from 14.9 to 7% after 6 months and remained at this level thereafter ($P = 0.12$). About one third of patients on rhGH experienced fluid-related adverse events, most often within the first 3 months. They usually disappeared spontaneously or responded well to dose reduction. Cumulative

dropout rates were 29% after 1 year and 38% after two years. Two thirds of these patients stopped treatment because of insufficient subjective improvement. Neither drop-outs nor fluid retention could not be predicted by any of the baseline parameters.

CONCLUSIONS: We confirmed in a large group of patients the beneficial effects of rhGH therapy on body composition, metabolic parameters and general well-being and found a consistent drop in number of sick days and hospitalization rate. These effects were maintained during two years of therapy, except for an attenuation in body composition changes after 24 months. The high incidence of fluid-related adverse events suggests that it may be better to start with lower doses of rhGH and to increase the dose more slowly over a number of weeks. The finding of suboptimal high or low IGF-1 levels in many patients reinforces guidelines not to give rhGH in a weight-dependent dose but to titrate it individually for each patient.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9404448&dopt=Abstract .