Recombinant Human Growth Hormone and Recombinant Human Insulin-Like Growth Factor 1 in Patients With HIV-Associated Wasting

Previous open-label studies of short duration have demonstrated that rhGH or rhIGF-1 increases body weight and lean body mass and decreases body fat in adults with wasting (> 10% weight loss) associated with HIV infection and AIDS.

Schambelan et al report that in a 12-week, randomized, double-blind, placebo-controlled multicenter study of 178 HIV-infected patients, rhGH (0.1 mg/kg/d; average dose, 6 mg/d) increased body weight (1.6 ± 3.7 kg), lean body mass (3.0 ± 3.0 kg), and total (2.4 ± 3.1 L) and intracellular (1.3 ± 2.9 L) body water, while there were no changes in these values in the placebo group. Body fat declined (-1.7 ± 1.7 kg) in rhGH-treated patients, but did not decrease significantly in the placebo-treated patients. In the rhGH-treated group, treadmill work output increased an average of 13.2% after 12 weeks. The perceived health status or use of health facilities in rhGH-treated subjects did not change. rhGH was reasonably well tolerated, but many patients developed edema, arthralgia, and diarrhea. The authors concluded that rhGH could partially reverse the wasting associated with HIV infection, but this was not accompanied by a subjective improvement or alteration in disease status.

Waters et al conducted a double-blind study of the effect 12 weeks of administration of rhGH (1.4 mg/d, or one quarter of the dose utilized in the first study); rhIGF-1 (5 mg twice daily); rhGH with rhIGF-1; or placebo in 60 patients with AIDS-associated wasting. In part because of a large dropout rate, these workers noted only transient increases in body weight and lean body mass and decline in fat mass in the groups receiving rhGH or rhIGF-1 alone; in the group receiving rhGH plus rhIGF-1 these changes persisted for 12 weeks. Increase in muscle strength and improvement in quality of life also were transient. In neither study was there any alteration in immune function or exacerbation of AIDS. Waters et al concluded that rhGH and rhIGF-1 at the doses employed in their study were not useful in the treatment of the wasting of AIDS.

Waters D, et al. Recombinant human growth hormone, insulin-like growth factor 1, and combination therapy in AIDS-associated wasting: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1996;125:865-872.

Schambelan M, et. al. Recombinant human growth hormone treatment and HIV-associated wasting. *Ann Intern Med* 1996;125:873-882.

Editor's comment: *Although rhGH, rhIGF-1, or a combination of the 2 agents can increase lean body mass and decrease body fat content in adults with HIV- and AIDS-associated wasting (at least transiently), beneficial effects on the course of the disease or the quality of life were not observed in either of the 2 studies. Despite such data, the Food and Drug Administration has approved a 12-week course of rhGH therapy for patients with HIV-associated wasting. The estimated cost per patient is $12,000.*

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Adult Height in Growth Hormone Deficiency (GHD) Children Treated With Biosynthetic GH

This study consists of the largest number of patients (121) treated over the longest period with a constant dose (0.3 mg/kg/wk) of rhGH reported to date. One hundred six patients completed the study and attained their adult height. The chronologic age at initiation of therapy was 11.3 ± 2.1 years for males and 10.1 ± 2.8 years for females. The etiology of GHD was 102 idiopathic versus 19 organic. Eighty-four of the 121 developed puberty spontaneously. The total duration of GH treatment (with or without native pituitary GH) was approximately 7.5 ± 3.2 years. The Bayley-Pinneau predicted adult height was 163.2 ± 7.4 cm for males and 150.0 ± 7.0 cm for females. The adult statistics are recorded in the table to the right.

Adult height was dependent on height (positively) and age (negatively) at the start of these protocols, duration of treatment on protocol, growth rate during first year, and sex.

The authors postulate that the significant increase in adult height over pretreatment predicted adult height may be due to larger doses of uninterrupted GH treatment than that used in previous studies. The authors also found, in contrast to previous studies, that spontaneous puberty or female sex did not adversely affect the adult height SDS, which improved significantly during puberty from

Adult Height in Subjects Treated With rhGH

Outcome Variable	Males (n=72)	Females (n=49)
Adult height (cm)[a]	171.6 ± 8.2	158.5 ± 7.1
Total height gained (cm)[b]	46.6 ± 11.8	41.6 ± 16.5
Adult height SD score	-0.7 ± 1.3	-0.7 ± 1.1
Adult height SD score minus midparental target height SD score[c]	-0.6 ± 1.2(n=66)	-0.4 ± 1.2 (n=45)
Age at onset of puberty[a]	14.0 ± 1.9	12.6 ± 2.2
Height at start of puberty (cm)[a]	146.7 ± 10.5	139.1 ± 11.8
Height SD score at start of puberty	-1.9 ± 1.2	-1.9 ± 1.5
Adult height minus predicted adult height at start of treatment (cm)[b]	8.5 ± 8.1	8.5 ± 7.1

Values are the mean ± SD.
[a] By *t* test, $P<0.0003$, males versus females.
[b] By paired *t* test, each sex, $P<0.0001$ (different from 0).
[c] By paired *t* test: females, $P=0.02$; males, $P<0.0001$ (different from 0)