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The Individual Responsiveness to Growth Hormone (GH) Treatment in GH-Deficient Adults Is Dependent on the Level of GH-Binding Protein, Body Mass Index, Age, and Gender*

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ABSTRACT

The aim of the present trial was to study the individual responsiveness to GH treatment in terms of body composition and to search for possible predictors of the response in GH-deficient adults.

Sixty-eight patients (44 men and 24 women) with a mean age of 44.3 (1.2) yr and verified GH deficiency participated in a 2-phase treatment trial with an initial randomized, double blind, placebo-controlled, 6-month period, followed by an open treatment period, thereby ensuring all patients 12 months of GH treatment.

Recombinant human GH was administered sc daily at bedtime, with a target dose of 12 μg/kg·day. GHBP was measured by ligand-mediated immunofunctional assay, and serum insulin-like growth factor I (IGF-I) was determined by RIA after acid-ethanol extraction, using a truncated IGF-I analog as the radioligand. Lean body mass (LBM) and body fat (BF) were determined by dual energy x-ray absorptiometry, and total body water (TBW) was determined by bioelectrical impedance.

During the placebo control period, serum IGF-I, LBM, and TBW increased ($P < 0.001$), whereas BF decreased ($P < 0.001$) and serum GHBP was unchanged in the group treated with GH compared with the patients treated with placebo. After 12 months of GH treatment, the individual changes in BF ranged from −12.5 to 4.3 kg and from −4.5 to 10.1 kg in LBM. Age ($P < 0.05$) and baseline GHBP level ($P < 0.01$) were inversely correlated with the increase in LBM. The GH-induced increment in IGF-I and TBW was greater in men than in women ($P < 0.01$), whereas the decreases in BF were similar in men and women.

This trial demonstrates the variability in responsiveness to GH administration in GH-deficient adults. The best response to GH was obtained in younger patients with low GHBP levels. Furthermore, men responded better than women. (*J Clin Endocrinol Metab* **81:** 1575–1581, 1996)

GH DEFICIENCY in adults is associated with impaired psychological well-being, abnormal body composition, metabolic abnormalities (1), and increased cardiovascular mortality (2). Several of these abnormal features tend to normalize during GH treatment (1). It has long been known that there is a considerable variability in the response to GH treatment in GH-deficient children (3), whereas less is known about the variation in GH responsiveness in GH-deficient adults. The clinical impression from the accumulating experience of treating GH-deficient adults indicates a highly individual variability in GH responsiveness. Several factors, such as gender, age, and whether the GH deficiency began in childhood or in adult life, could influence the response to GH treatment. Furthermore, serum GH-binding protein (GHBP), which is a high affinity binding protein (4, 5) suggested to be produced by proteolytic cleavage of the extracellular domain of the GH receptor (6, 7), may reflect the tissue level of GH receptors and the responsiveness to GH. GHBP prolongs the biological half-life of GH and decreases the distribution volume of GH in the body (8); in GH-treated GH-deficient children, GHBP levels correlated positively with the increment in serum insulin-like growth factor I (IGF-I) and growth velocity (9). Hence, serum GHBP levels may have a regulatory effect on GH responsiveness during GH treatment in adults with GH deficiency.

In the present study, we demonstrate the individual responsiveness to GH in terms of body composition changes and search for possible predictors of the variable response to GH treatment in GH-deficient adults.

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Subjects and Methods

Patients

Sixty-eight adults with known pituitary deficiency and a mean age of 44.3 ± 1.2 (±se) yr from 3 referral centers in Sweden participated: Sahlgrenska University Hospital, Göteborg (25 patients); Malmö University Hospital, Malmö (23 patients); and Karolinska Hospital, Stock-

holm (20 patients). The mean duration of pituitary deficiency was 15.2 ± 1.1 yr, and it was most frequently caused by pituitary tumors (Table 1). The diagnosis of GH deficiency was based upon a maximum peak GH response of less than 10 mIU/L during a stimulation test performed within 5 yr before inclusion in this study, using insulin hypoglycemia in 25 subjects, glucagon in 22, clonidine in 19, and arginine in 2 subjects. The mean peak response was 1.11 ± 0.15 mIU/L (range, 0.00–6.00). All adults with childhood-onset pituitary deficiency were retested before entering the trial. One center (Karolinska Hospital) also used a low serum IGF-I concentration as a screening test for GH deficiency. When required, patients received adequate and stable replacement therapy with glucocorticoids (cortisone acetate, 10–37.5 mg/day), thyroid hormone (levothyroxine, 0.1–0.2 mg/day), gonadal steroids, and desmopressin for at least 6 months before inclusion in the study. Replacement therapy was kept constant during the study period in all patients except 1 man, for whom the levothyroxine dosage was increased from 0.05 to 0.15 mg/day after 6 months of GH treatment due to low free T_4 concentrations.

Study protocol

The study was designed as a two-phase treatment trial, with an initial randomized, placebo-controlled, double blind, 6-month period, followed by a period of open treatment for 6 or 12 months, thereby ensuring all patients a total treatment period of 12 months with GH. Informed consent was obtained from each patient before the study. The study was approved by the ethics committees of the Karolinska Institute and the Medical Faculties at the University of Goteborg and the University of Lund and by the Swedish Medical Products Agency.

During the first 4 weeks of treatment, in both the placebo-controlled period and the period of open treatment, the daily GH dose was 6 μg/kg (0.125 IU/kg·week), and the target dose thereafter was 12 μg/kg (0.25 IU/kg·week). The dose was reduced in the event of side-effects, and as a result, the mean dose of GH was reduced after both 6 and 12 months of treatment compared with the target dose at 1 month. The dose reduction was similar in men and women as well as in patients with childhood and adult-onset pituitary deficiency. Recombinant human GH (Genotropin, Pharmacia, Uppsala, Sweden) was used. The placebo vials contained the same vehicle as the GH vials and were visually indistinguishable.

The patients were studied on an out-patient basis. At the start and every subsequent 6 months, physical and laboratory examinations were performed, including determination of body composition. In addition, the patients were given a physical examination and safety laboratory investigation every 3 months.

During the 6-month placebo-controlled treatment period, 3 patients discontinued treatment: a 31-yr-old man developed noninsulin-dependent diabetes mellitus after 3 months of active treatment, a 35-yr-old woman discontinued treatment after 1 month because of peripheral edema and musculoskeletal pain, and an 18-yr-old woman was excluded because of noncompliance. During the period of open treatment, a 53-yr-old man from the placebo group discontinued treatment after 6 months of GH therapy because he experienced no positive effects. Thus, 65 patients were available for analysis after the 6-month placebo-controlled period, and 64 patients were available after the 12-month treatment.

Body composition

Body weight was measured to the nearest 0.1 kg using a Stathmos balance in the morning after fasting overnight and after the patient had urinated. Body height was measured to the nearest 0.01 m. The body mass index (BMI) was calculated as body weight (kilograms) divided by height (meters) squared.

Body composition was determined by bioelectrical impedance (BIA) and dual energy x-ray absorptiometry (DEXA). DEXA was performed using a whole body scanner (Lunar DPX, Scanexport Medical, Helsingborg, Sweden) according to a standard procedure described previously (10). The same type of calibration phantom (Lunar) was used at all participating centers. The coefficient of variation (CV) was 4% for body fat (BF) and 1.6% for lean body mass (LBM) (10). BIA was measured in the supine position using BIA-101 equipment (RJL System, Detroit, MI) according to the manufacturer's instructions. A 50-kilohertz, 800-microampere current was applied. Total body water (TBW) was calculated from equations supplied by the manufacturer based on comparisons with densitometry in a normal population. The BIA measurements had a day to day CV of 1.7% (11).

Biochemical assays

Blood samples were drawn in the morning after an overnight fast. Serum IGF-I was determined by RIA after acid-ethanol extraction. A truncated IGF-I analog [des-(1–3) recombinant human IGF-I] was used as a radioligand to minimize the influence of IGF-binding proteins (12). The level of detection was 20 μg/L, and the intra- and interassay CVs were 3.1% and 10.0%, respectively.

Serum GHBP was measured using a ligand-mediated immunofunctional assay (LIFA), as described previously (13). The detection range in the LIFA was 15.6–1000 pmol/L, and the intraassay CV was 7.3%.

Statistical methods

All descriptive statistical results are presented as the mean and SEM. Fisher's permutation test was used to compare both baseline values and

TABLE 1. Characteristics of the cohort of 68 patients with GH deficiency included in the study

Patient characteristics	All	GH group	Placebo group	Men	Women	Adult onset	Childhood onset[a]
No. of subjects (male/female)	68	34 (18/16)[b]	34 (26/8)	44	24	47 (29/18)	21 (15/6)
Mean age (yr)[c]	44.3 (1.2)	44.7 (1.8)	43.8 (1.8)	44.1 (1.5)	44.6 (2.1)	47.6 (1.4)[d]	36.9 (1.6)
Known duration of pituitary deficiency (yr)[c]	15.2 (1.1)	16.3 (1.5)	14.1 (1.7)	14.4 (1.4)	16.7 (2.0)	11.5 (1.2)[d]	23.4 (1.6)
Causes of pituitary deficiency							
Nonsecreting adenoma	31	15	15	14	16	25[e]	5
Prolactinoma	8	3	5	7	1	7	1
Craniopharyngioma	13	9	5	12	2	7	7
Idiopathic	9	4	5	6	3	2	7
Others	7	3	4	5	2	6	1
Hormonal replacement therapy							
Cortisone acetate	61	31	30	41	20	43	18
Levothyroxine	61	33	28	40	21	43	18
Gonadal steroids	63	32	31	41	22	45	18
Isolated GH deficiency	3	1	2	1	2	1	2
Desmopressin	19	11	8	13	6	13	6

[a] Onset of pituitary deficiency before the age of 20 yr.
[b] $P < 0.05$ *vs.* placebo group in terms of the number of men and women.
[c] Values are expressed as the mean (SEM).
[d] $P < 0.001$ *vs.* the group with childhood-onset GH deficiency.
[e] $P < 0.05$ *vs.* the group with childhood-onset in terms of the causes of pituitary deficiency.

individual differences in response to GH treatment in the various subgroups of patients. Fisher's test of paired comparisons was used to test for differences between baseline and 6 and 12 months values during the 12-month open treatment period. When significant differences between subgroups were found at baseline, the influence of these differences on the treatment response was tested using Mantel's test. Correlations between GHBP, IGF-I, BMI, and age at baseline and the treatment response measured by DEXA were sought using Pitman's test. Where statistical significance was obtained, Pearson's correlation coefficient was calculated. If more than one baseline variable reached significance, these variables were tested simultaneously using a standard multiple regression analysis. A two-tailed $P < 0.05$ was considered significant.

Results

During the placebo-controlled treatment period, serum IGF-I, LBM, and TBW increased, and BF decreased in the GH-treated patients compared with those in the placebo-treated patients (Table 2). These changes persisted during the 12 months of open treatment (Table 3). No significant change occurred in the GHBP concentration in the GH-treated group compared with the placebo group (Table 2), whereas after 12 months of treatment in the entire treatment group, the serum GHBP concentration decreased by 7% compared with the baseline value (Table 3).

The individual responsiveness to GH treatment varied, as demonstrated in Table 3 and Fig. 1. The average GH dose of 11 ± 0.2 μg/kg·day (range, 6–13) during the 12 months of treatment correlated with the increment in serum IGF-I concentration (r = 0.40; $P < 0.01$), but not with the changes in BF (r = −0.12; P = NS) and LBM (r = 0.14; P = NS).

There was a positive correlation between the baseline BMI and the change in BF between baseline and 12 months (r = 0.28; $P < 0.05$) of GH treatment. Both the baseline GHBP concentration (r = −0.36; $P < 0.01$) and age (r = −0.25; $P < 0.05$) correlated inversely with the change in LBM. Both correlations persisted in a multiple regression analysis using change in LBM as dependent variable (Fig. 2). Furthermore, both baseline BMI (r = −0.40; $P < 0.001$) and baseline GHBP concentrations (r = −0.47; $P < 0.001$) correlated negatively with the change in the lean/fat ratio. However, when included in a multiple regression analysis using change in the lean/fat ratio as the dependent variable, only the GHBP concentration continued to be significantly correlated with the increase in lean/fat ratio (Fig. 3). However, no correlation was found between the baseline GHBP levels and the change in the serum IGF-I concentration (r = 0.14; P, NS). The baseline serum IGF-I concentration did not correlate with the treatment response, measured as the increments in IGF-I (r = 0.02; P, NS) and LBM (r = 0.06; P, NS) and the decrease in BF (r = 0.12; P, NS). Eight patients (five men and three women; mean age, 43.0 ± 3.0 yr) did not respond to GH treatment in terms of the expected changes in body composition. Although demonstrating an increase in serum IGF-I concentration from 68 ± 8 to 268 ± 24 μg/L ($P < 0.01$) after 12 months of treatment, BF increased from 31.1 ± 2.9 to 32.9 ± 3.0 kg ($P < 0.05$), and LBM and TBW were unchanged. Compared with the responders, this group of patients had higher BMI (30.4 ± 1.6 *vs.* 25.5 ± 0.8 kg/m^2; $P < 0.05$) and tended to have increased GHBP concentrations (416 ± 53 *vs.* 311 ± 21 pmol/L; $P = 0.09$) at baseline.

At baseline, a positive correlation was found between the serum GHBP concentration and both BMI (r = 0.55; $P < 0.001$) and BF (r = 0.57; $P < 0.001$; Fig. 4A), but not between GHBP and LBM (r = 0.16; P = NS), IGF-I (r = 0.15; P = NS), or age (r = 0.04; P = NS). After 12 months of GH treatment, a positive correlation was found between the GH-induced decrease in BF and the decrease in GHBP (r = 0.38; $P < 0.05$) between baseline and 12 months (Fig. 4B).

Adult- vs. childhood-onset pituitary deficiency

Before treatment, patients with childhood-onset disease had lower serum IGF-I concentration (40 ± 5 *vs.* 64 ± 5 μg/L; $P < 0.05$), body height (1.66 ± 0.02 *vs.* 1.73 ± 0.01 m; $P < 0.01$), LBM (44.8 ± 2.5 *vs.* 51.2 ± 1.7 kg; $P < 0.05$), and TBW (36.4 ± 1.8 *vs.* 42.0 ± 1.2 kg; $P < 0.05$) than patients with adult-onset disease, whereas the BF mass and serum GHBP con-

TABLE 2. Serum IGF-I, GH-binding protein (GHBP), and body composition in adults with GH deficiency treated with rhGH (n = 32) or placebo (n = 33) for 6 months

Variable	Group	Baseline	6 months	Mean changes
Serum IGF-I (μg/L)	GH	57 (7)	211 (18)	157 (17)[a]
	Placebo	62 (6)	60 (5)	−2 (3)
GHBP (pmol/L)	GH	309 (26)	300 (28)	−10 (19)
	Placebo	333 (32)	342 (30)	−38 (39)
Body mass index (kg/m^2)	GH	27.8 (1.2)	27.4 (1.2)	−0.4 (0.2)[b]
	Placebo	26.0 (0.8)	26.2 (0.8)	0.2 (0.2)
Body fat (kg)	GH	26.4 (2.0)	23.9 (2.1)	−2.6 (0.4)[a]
	Placebo	23.0 (1.3)	23.4 (1.5)	0.4 (0.3)
Lean body mass (kg)	GH	46.8 (2.2)	48.8 (2.2)	2.0 (0.3)[a]
	Placebo	51.4 (1.8)	51.7 (1.8)	0.3 (0.2)
Total body water (kg)	GH	38.9 (1.6)	40.6 (1.7)	1.6 (0.3)[a]
	Placebo	41.6 (1.4)	41.8 (1.4)	0.1 (0.2)

Values are expressed as the mean (SEM).
[a] $P < 0.001$ compared with changes in the placebo-treated group.
[b] $P < 0.05$ compared with changes in the placebo-treated group.
[c] $P < 0.05$ compared with changes in the placebo-treated group.

TABLE 3. Serum IGF-I, GH-binding protein (GHBP), and body composition in 64 adults with GH deficiency treated with rhGH for 12 months

Variable	Baseline	6 months	12 months	Changes	
				Mean	Range
Dose rhGH (μg/kg · day)	12 (0.00)[a]	11 (0.3)[b]	10 (0.3)[b]	2 (0.3)	−8.8 to 1.9
IGF-I (μg/L)	56 (4)	231 (13)[b]	254 (13)[b]	198 (12)	−22 to 398
GHBP (pmol/L)	324 (20)	296 (20)[c]	300 (20)[c]	−24 (11)	−254 to 181
Body mass index (kg/m^2)	27.0 (0.7)	26.7 (0.7)	27.0 (0.8)	0.01 (0.17)	−4.1 to 3.7
Body fat (kg)	25.0 (1.2)	22.3 (1.3)[b]	23.0 (1.4)[b]	−2.0 (0.4)	−12.5 to 4.3
Lean body mass (kg)	49.2 (1.4)	51.2 (1.5)[b]	51.5 (1.5)[b]	2.4 (0.3)	−4.5 to 10.1
Lean/fat ratio	2.23 (0.11)	2.78 (0.17)[b]	2.73 (0.17)[b]	0.51 (0.09)	−0.25 to 3.26
Total body water (kg)	40.2 (1.1)	42.4 (1.1)[b]	42.0 (1.1)[b]	1.8 (0.2)	−2.2 to 6.7

Values are expressed as the mean (SEM).
[a] The mean dose of rhGH at 1 month of treatment.
[b] $P < 0.001$ compared with baseline levels.
[c] $P < 0.05$ compared with baseline levels.

centration were similar in the 2 groups. However, when the difference in height between the groups was taken into consideration using Mantel's test, only the difference in serum IGF-I concentration remained significant between the groups ($P < 0.05$). However, this difference could be explained by the fact that 13 of 21 patients with childhood-onset pituitary deficiency were included at the center using a lower serum IGF-I concentration as a screening method for GH deficiency. During the 12-month treatment period, the increase in serum IGF-I concentration and the changes in body composition were similar in the 2 groups (data not shown).

Men vs. women

At baseline, LBM, lean/fat ratio, and TBW were higher in men than in women, but BF values were similar in the two groups (data not shown). The increase in the serum IGF-I concentration (227 ± 15 *vs.* 151 ± 17 μg/L; $P < 0.01$) and TBW (2.3 ± 0.3 *vs.* 0.9 ± 0.3 kg; $P < 0.01$) after 12 months of GH treatment was more pronounced in men, even after making adjustments for gender differences in body composition at baseline. The changes in BF and LBM, however, were similar in men and women. The GHBP concentration at baseline and the change in GHBP in response to treatment were similar for both genders.

Discussion

Variability in the response to GH treatment in GH-deficient adults has been suspected, but not previously documented. This trial was, therefore, conducted to describe the individual responsiveness to GH treatment and to search for possible predictors of the response in a heterogeneous group of GH-deficient adults. To summarize, a highly individual responsiveness to GH administration in GH-deficient adults was found, which was explained to some extent by differences in baseline BMI, baseline serum GHBP levels, age, and gender. Patients with a high BMI, thus, experienced a lower reduction in BF, and patients with low baseline GHBP levels demonstrated the most marked increase in LBM and lean/fat ratio. Younger patients displayed a more marked increase in LBM, whereas the GH-deficient men experienced a more pronounced increase in serum IGF-I concentration and TBW than the women.

The serum GHBP concentration was similar in our group

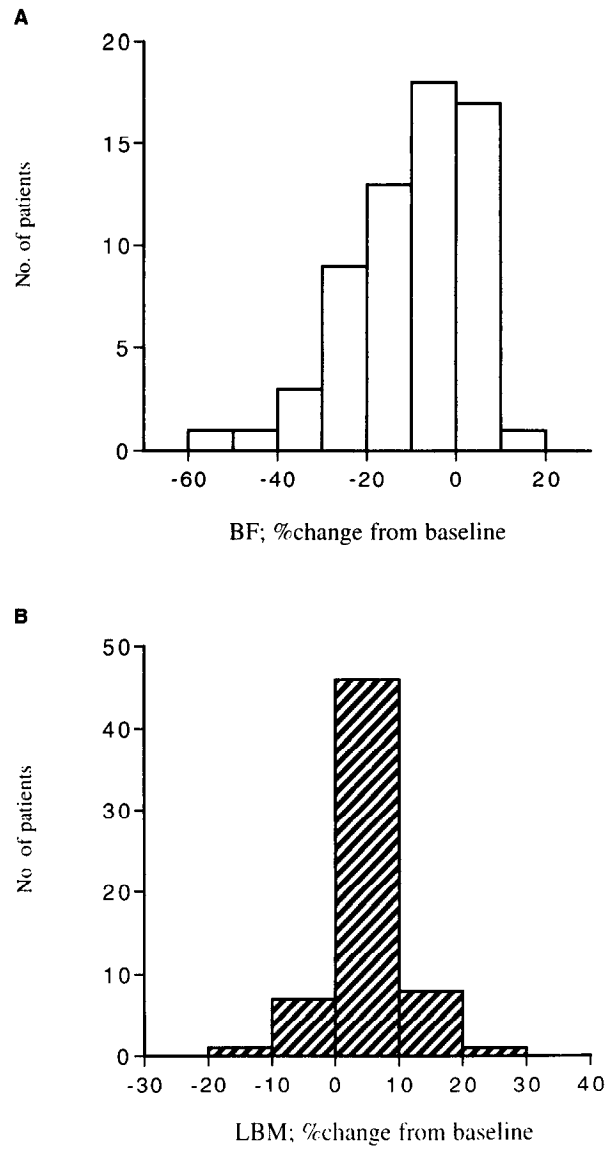
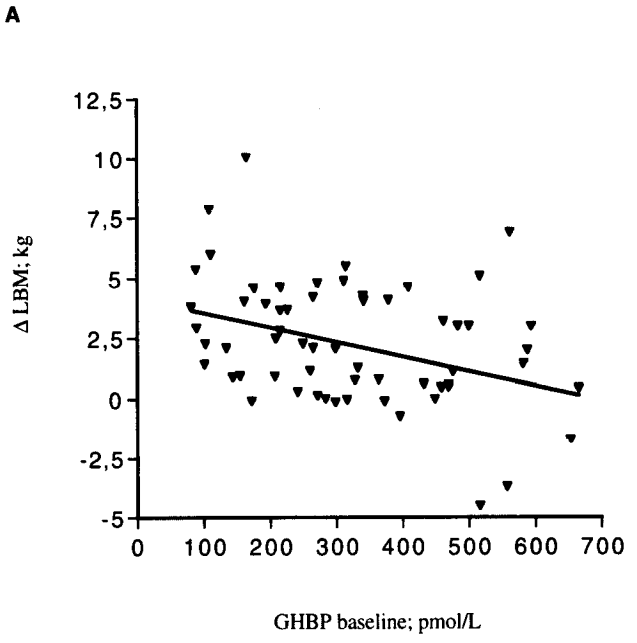


FIG. 1. Variability in body composition changes in response to GH treatment in 64 adults with GH deficiency. The response to treatment is expressed as the percent changes after 12 months of GH treatment compared with baseline in BF (A) and LBM (B) assessed by DEXA.



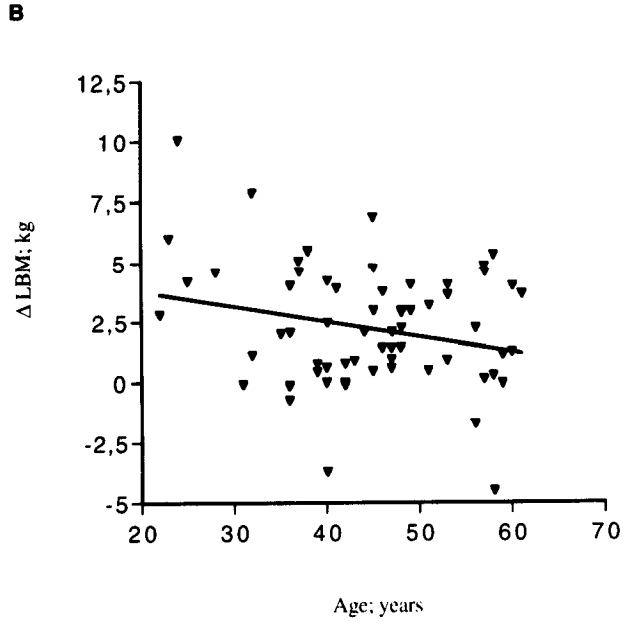


FIG. 2. The correlation among age, baseline GHBP concentration, and change in lean body mass (Δ LBM) in 64 GH-deficient adults treated with GH for 12 months. The equation for the regression line is Δ LBM = 6.935 − 0.006 × GHBP − 0.06 × age ($r = 0.43$; $P < 0.01$). A, Correlation between GHBP at baseline and Δ LBM when age is kept constant at 45 yr. B, Correlation between age and Δ LBM when GHBP is kept constant at 320 pmol/L.

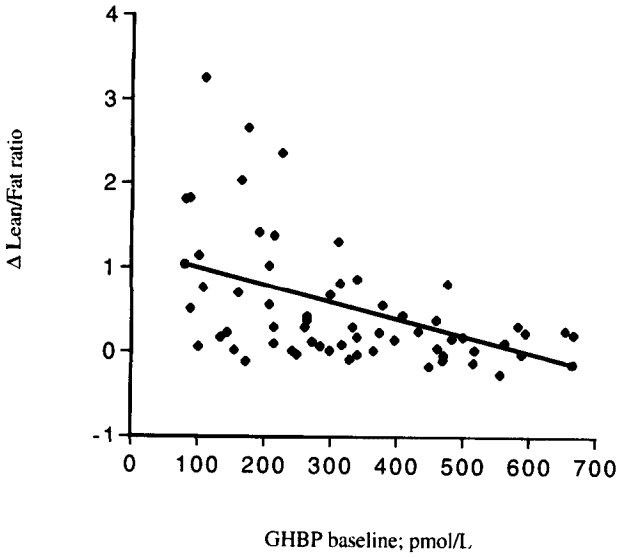


FIG. 3. The correlation between serum GHBP concentration at baseline and changes in lean/fat ratio (Δ Lean/Fat ratio) in 64 GH-deficient adults treated with GH for 12 months. The equation for the regression line is Δ lean/fat = 1.202 − 0.002 × GHBP ($r = -0.47$; $P < 0.001$).

of GH-deficient adults to the levels previously described in normal adults (14). The positive association between BMI and GHBP levels previously described in both adults (15) and normal boys (16) was also found in this group of GH-deficient adults. However, as BMI is a function of both height and weight, and body weight is composed of both BF and LBM, the level of GHBP could be associated with BF, LBM, or both. Our results, however, only showed a correlation between BF and GHBP. This can be demonstrated in patients with acromegaly, who have decreased BF, increased LBM (17), and lower levels of serum GHBP than healthy adults (14) despite having a high BMI (17). Furthermore, the relationship between the reduction in BF and the slight reduction in GHBP levels during GH treatment suggests that the decrease in the serum GHBP concentration in response to GH administration merely reflects the decrease in the amount of BF. Previous studies have also suggested the importance of nutritional factors to GHBP levels (15, 18). As the liver is presumed to be the primary site of GHBP synthesis (19), it is conceivable that the production of GHBP from the liver is increased in response to adiposity, possibly through some common metabolic pathway, such as insulin (20–22). An alternative explanation could be that the GHBP produced by the adipose tissue is a major contributor to the circulating levels of GHBP. This is supported by the fact that GH receptor expression in adipose tissue in the rat is higher than that in muscle tissue (23). Moreover, although the abundance of the GH receptor is greater in liver than in fat, the total body fat mass is higher than the liver mass.

To date, this is the largest reported treatment trial describing the previously documented changes in body composition in response to GH administration in GH-deficient adults (1). Interestingly, patients with a higher BMI experienced a less pronounced reduction in BF in response to GH administration. This observation contradicts a previous study of GH-deficient children that demonstrated a positive correlation between baseline BMI and the response to GH treatment in terms of growth velocity and serum IGF-I increment (24). Furthermore, in the present trial, an inverse relationship was found between the baseline serum GHBP concentration and the increase in LBM and lean/fat ratio in response to GH treatment. This is also in contrast to a previous finding in GH-treated, GH-deficient children (9), in whom the baseline GHBP levels correlated positively with the response to GH

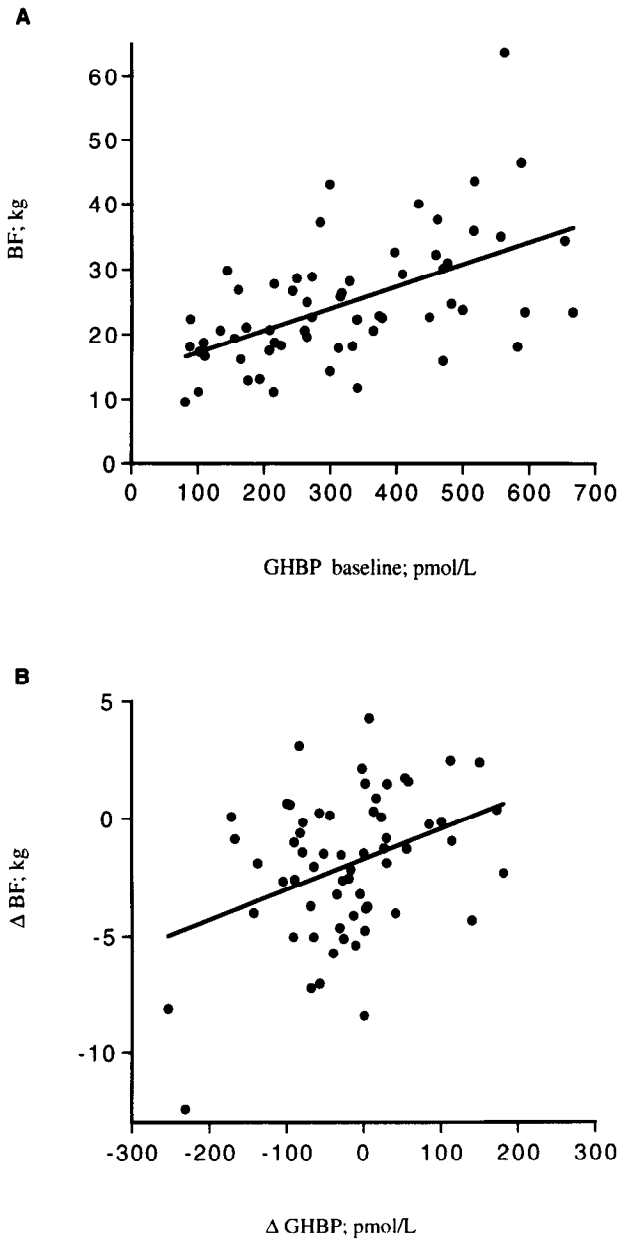


FIG. 4. The correlation between serum GHBP concentration and BF in 64 GH-deficient adults treated with GH for 12 months. A, Correlation between baseline serum GHBP concentration and baseline BF. The equation for the regression line is BF = 13.905 + 0.03392 × GHBP ($r = 0.55$; $P < 0.001$). B, Correlation between changes in serum GHBP concentration (Δ GHBP) and changes in BF (Δ BF). The equation for the regression line is Δ BF = −1.685 + 0.013 × Δ GHBP ($r = 0.38$; $P < 0.05$).

administration in terms of growth velocity and IGF-I increment. However, in children with idiopathic short stature, no significant correlation between GHBP levels and growth response to exogenous GH was found (25). The present results, however, are in line with *in vitro* experiments that demonstrate a dampening effect by GHBP on GH binding to cells and on GH-dependent IGF-I production (26, 27). These discrepancies could be explained by the different effects of GHBP, acting as a competitor to the GH receptor for the binding of GH and prolonging the circulating half-life of GH (8). Furthermore, different subjects, tissues, and end points might explain the converse effect of serum GHBP on the response to GH administration.

The apparent differences in body composition between subjects with adult- and childhood-onset GH deficiency at baseline were explained by the lower body height in the adults with childhood-onset disease. The GHBP levels and response to GH treatment in terms of body composition and serum IGF-I concentration were, however, similar in patients with childhood- and adult-onset GH deficiency, indicating that the GHBP/GH receptor environment does not differ significantly between these groups.

The observed gender difference in body composition at baseline is the same as that in healthy adults (28), but a gender difference in the response to GH in GH-deficient adults has not been described previously. The importance of gonadal steroids on body composition is well known (29). Thus, the different response to GH in GH-deficient men and women is most likely explained by different interactions between GH *vs.* estrogens and androgens, respectively, on body composition. The less pronounced increase in serum IGF-I seen in women could be an effect of the previously described IGF-I-lowering properties of estrogen (30, 31). Testosterone treatment increases serum IGF-I concentrations in normal men and in men with isolated hypogonadotropic hypogonadism (32, 33). However, this increment is probably mediated through increased endogenous GH secretion in subjects with intact pituitaries (33) and, therefore, cannot explain the gender differences in IGF-I in this study. This is further supported by a study of hypophysectomized rats that demonstrated no effect on IGF-I gene expression or serum IGF-I concentration during testosterone administration (34).

This study demonstrates that the level of GHBP was dependent on the amount of BF both before and during GH treatment and, thus, demonstrates the importance of taking account of body composition when studying serum levels of GHBP in various clinical conditions. Moreover, this study describes a considerable variability in responsiveness to GH in GH-deficient adults in terms of body composition, which was explained to some extent by the serum GHBP level, BMI, age, and gender. This study, therefore, emphasizes the importance of considering each patient individually during GH replacement therapy.

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