Effect of growth hormone treatment on hormonal parameters, body composition and strength in athletes

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The effect of recombinant GH on strength, body composition and endocrine parameters in power athletes was investigated in a controlled study. Twenty-two healthy, non-obese males (age 23.4 ± 0.5 years; ideal body weight 122 ± 3.1%, body fat 10.1 ± 1.0%; mean ± SEM) were included. Probands were assigned in a double-blind manner to either GH treatment (0.09U (kg BW)⁻¹ day⁻¹ sc) or placebo for a period of six weeks. To exclude concurrent treatment with androgenic-anabolic steroids urine specimens were tested at regular intervals for these substances. Serum was assayed for GH, IGF-I, IGF-binding protein, insulin and thyroxine before the onset of the study and at two-weekly intervals thereafter. Maximal voluntary strength of the biceps and quadriceps muscles was measured on a strength training apparatus. Fat mass and lean body mass were derived from measurements of skinfolds at ten sites with a caliper. For final evaluation only data of those 8 and 10 subjects in the two groups who completed the study were analyzed. GH, IGF-I and IGF-binding protein were in the normal range before therapy and increased significantly in the GH-treated group. Fasting insulin concentrations increased insignificantly and thyroxine levels decreased significantly in the GH-treated probands. There was no effect of GH treatment on maximal strength during concentric contraction of the biceps and quadriceps muscles. Body weight and body fat were not changed significantly during treatment. We conclude that the anabolic, lipolytic effect of GH therapy in adults depends on the degree of fat mass and GH deficiency. In highly trained power athletes with low fat mass there were no effects of GH treatment on strength and body composition.

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There is little information on the significance of growth hormone (GH) in adults and its effects after linear growth is completed. In growth hormone-deficient adult patients substitution with GH increased lean body mass and reduced fat mass (1, 2). A similar effect of GH treatment on body composition was seen in elderly people who have physiologically low GH concentrations (3). In adults without GH deficiency the results of short-term GH application were contradictory (4, 5) and only recently has it been demonstrated that GH has no additional effect on exercise-induced muscle growth and strength (6).

GH is reported to be used by bodybuilders and other athletes in order to increase muscle strength and weight gain without being detected by doping controls (7). However, there is no scientific evidence documenting an improvement in athletic performance following GH supplementation. We have therefore performed a double-blind placebo-controlled study on the effects of recombinant human GH (r-hGH) on physical and endocrine parameters in adult males undergoing regular strength training. Although GH and IGF-I concentrations increased significantly after GH therapy, there was no effect on muscle strength and body composition.

Subjects and methods

The 22 male power athletes who participated in the study were solicited locally from an athletes club. They ranged in age between 20 and 28 years (23.4 ± 0.5 years; mean ± SEM), the ideal body weight (IBW), which was calculated from published tables of the WHO (8), was 97–140% (122.5 ± 3.1%). Subjects were in good general health and had no history of diabetes, hypertension or disorder of GH secretion. They had performed regular weight training for at least six months prior to the study. During the study, neither the training regimen, which included 8–14 h of heavy resistance training per week nor the dietary intake was changed. The probands were on a low fat, high protein (1.5–2.5 g (kg BW)⁻¹ day⁻¹) and high caloric (45–55 kcal (kg BW)⁻¹ day⁻¹) regimen. To exclude concurrent treatment with androgenic-anabolic steroids urine specimens were tested before and during the study for these substances by gas chromatography and mass spectrometry as previously described (9).

Probands were assigned in a double-blind manner to either the GH (Genotropin, Kabi Pharmacia, Sweden) or the placebo group. The GH dose was 0.09 ± 0.001 U per
kilogram body weight daily, self-administered subcutaneously at bedtime. The placebo vials contained the same vehicle as the r-hGH vials and were indistinguishable from them. Compliance was assessed by counting the returned empty vials.

Blood samples for estimating the following parameters were taken in the morning in fasting condition before treatment was initiated and two, four and six weeks thereafter: GH, insulin-like growth factor I (IGF-I), IGF-II, IGF-binding protein 3 (IGFBP-3), insulin, thyroxine, free thyroxine, triiodothyronine, TSH, LH, FSH, testosterone, blood glucose, HbA1c, serum chemistry. During treatment blood samples were taken approximately 12 h after the last GH or placebo injection. At the same timepoints of the trial an evaluation of physical parameters (blood pressure, weight, skinfolds, strength from the biceps humeri and quadriceps femoris muscles) was performed.

Serum chemistry parameters were determined with a multichannel analyzer. HbA1c was determined by HPLC. Serum concentrations of hGH, LH, FSH, triiodothyronine, TSH, thyroxine, free thyroxine, insulin and testosterone were determined by standard radioimmunoassay methods. IGF-I and IGF-II were measured by radioimmunoassay after acid ethanol extraction as described earlier (10, 11). IGFBP-3 was measured by RIA as described in detail (12). Samples for hormone determinations were analyzed in the same assay.

Muscle strength was evaluated by using a sports-motoric test. Maximal voluntary strength during concentric contraction was measured by the one repetition maximum principle on a strength training apparatus (GYM 80, Essen, Germany). One repetition maximum is the maximal weight that can be lifted by specific muscle groups without use of momentum or change in body position. The coefficient of variation for 10 strength measurements in the same proband was 6.3%. The results of the strength tests were expressed in kilograms. Skinfold thickness was measured by the same person at 10 sites using a BEST caliper. The percentage of body fat was then calculated by the method of Parizkova (13). Lean body mass (LBM) was calculated by subtracting the fat mass from the body weight.

The results are reported as means ± SEM. To analyze changes of parameters during the course of the trial, and differences between the placebo and GH groups, analysis of variance with repeated measures was performed. In case of significant results between the placebo and GH groups, an additional two sample t-test with adjustment of the p-value by Bonferroni-Holm (14) was carried out.

The nature of the trial was explained to the athletes, and their written informed consent was obtained. The
Table 1. Fasting blood glucose, insulin levels and HbA1c, thyroxine, free thyroxine and triiodothyronine levels in the GH-treated and placebo-treated athletes before therapy (0) and after 2, 4 and 6 weeks of therapy.

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>6 weeks</th>
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<tr>
<td><strong>Fasting blood glucose (mmol/l⁻¹)</strong></td>
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<tr>
<td>rhGH</td>
<td>4.5 ± 0.03</td>
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<td>4.6 ± 0.2</td>
<td>4.8 ± 0.1</td>
<td>4.3 ± 0.1</td>
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<td><strong>Insulin (mU/l⁻¹)</strong></td>
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<tr>
<td>rhGH</td>
<td>12.1 ± 1.4</td>
<td>22.4 ± 5.2</td>
<td>27.4 ± 7.1</td>
<td>16.1 ± 0.8</td>
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<td><strong>HbA1c (%)</strong></td>
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<td>4.8 ± 0.1</td>
<td>5.0 ± 0.1</td>
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<td>5.0 ± 0.1</td>
<td>5.1 ± 0.26</td>
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<td><strong>thyroxine (mmol/l⁻¹)</strong></td>
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<td>93.9 ± 6.4</td>
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<td>81.0 ± 3.8</td>
<td>83.6 ± 5.1</td>
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<td>102.9 ± 5.1</td>
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<td>13.5 ± 1.2</td>
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<td>11.0 ± 0.6</td>
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<td>14.1 ± 1.2</td>
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<tr>
<td><strong>triiodothyronine (mmol/l⁻¹)</strong></td>
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* Significant at the 5% level.

Ethics Committee of the Medical Department of the University of Vienna reviewed the protocol and gave its consent.

Results

Eleven athletes received r-hGH and another 11 received placebo. Three probands of the r-hGH group dropped out and were excluded from evaluation; one of them had symptoms of carpal tunnel compression and fluid retention after one week of treatment and was unable to continue the study because of pain in the fingers. The other two probands, who had slight edema of the fingers, and one of the placebo group discontinued the trial on their own volition. For final evaluation there were 8 subjects in the rhGH group and 10 in the placebo group. Two probands of the r-hGH treated group experienced prominent edema in the fingers and pain during the first week of therapy, but these side effects resolved spontaneously despite continued treatment.

Basal GH levels were in the normal range and increased significantly after initiation of treatment in the rhGH group (p < 0.01). The levels after two and four weeks were significantly higher than in the placebo group (Fig. 1).

Serum concentrations of IGF-I were in the upper normal range and increased in the GH-treated subjects (p < 0.001). These levels were significantly higher than those in the placebo group after 2, 4 and 6 weeks (Fig. 1) and were above the age-related normal range (15). A similar course was seen in IGFBP-3 concentrations, the major binding protein of IGF-I; basal levels were in the normal range and increased with GH treatment (p < 0.001). The levels were significantly higher than in the placebo group (Fig. 1).

IGF-II levels were in the age-related normal range and did not change during GH therapy. IGF-I and IGFBP-3 increased in each individual patient of the GH-treated group, which can be taken as an additional monitor for the compliance of the probands.

Serum thyroxine levels decreased in the GH treated group (p < 0.05) and were different from those in the control group at four weeks. Serum levels of free thyroxine showed the same course, but the decrease was not significant. Triiodothyronine concentrations increased in the GH-treated group (p < 0.05) and were different from those in the control group at 2, 4 and 6 weeks (Table 1).

Serum TSH, LH and FSH and testosterone levels were in the normal range and did not change during the study period in any group (data not shown). Fasting insulin levels and blood glucose levels tended to be higher in the GH treated group after initiation of therapy (ns) and HbA1c remained unchanged (Table 1).

There was no significant change of serum cholesterol, triglycerides and serum chemistry during the study in either group.

IBW was insignificantly different in the two groups
before and during the trial, but there was no significant effect of GH therapy on body weight.

Also, maximum concentric strength of the biceps brachii and quadriceps femoris muscles was insignificantly higher in the GH-treated group already before the start of the trial. There was a significant increase in strength versus pretreatment values in both groups (p < 0.01 for biceps, p < 0.05 for quadriceps muscles). However, this increase was identical in the GH-treated group and in the placebo group and has to be considered as a training effect (Fig. 2). The differences between the two groups in weight and muscle strength, which were present already at the onset of the study, became obvious only after breaking the code and could not be avoided due to the double-blind design of the study. However, changes of the investigated parameters during the course of the study were analyzed by analysis of variance and were therefore not affected by these differences.

Fat mass was as low as 10.0 and 8.2 kg in the two groups (ns), respectively, before therapy and was not affected by treatment (Fig. 3).

Lean body mass was slightly different in the two groups, but it was not affected by GH therapy during the course of the trial (Fig. 3).

At urinary controls in each subject before and during the trial no relevant amounts of androgenic-anabolic steroids were detected.
Discussion

Recent studies in adult patients with GH-deficiency have shown that the disease-specific alterations in body composition like increased fat mass and decreased lean body mass can be reversed by replacement with GH substitution (2, 16). In addition, isometric muscle strength, exercise capacity and muscular volume (measured by CT) improved significantly after GH administration in conventional replacement doses in hypopituitary patients (2). A similar effect of GH treatment on body composition was seen in healthy, aged probands who had physiologically low IGF-I concentrations and a higher percentage of body fat similar to GH-deficient patients (3). In contrast, in healthy, trained subjects only a small change in body composition was seen after GH administration (4). In obese subjects who had caloric restriction, GH therapy produced no additional fat loss, and strength as measured by a tensiometer increased insignificantly (5).

We have treated highly trained athletes with GH in a double-blind placebo-controlled study in order to see whether muscle strength and body composition can be influenced by GH administration. Since GH can produce muscular growth in the absence of muscular work and work-induced growth can occur in the absence of pituitary hormone (17), it appears that muscle growth is a function of both work and hormonal factors. In our probands muscle growth was maximally stimulated by continuous intensive physical training, resulting in an ideal body weight of 122%, with a fat mass of only 10%.

Basal GH levels were normal and IGF-I concentrations, which reflect integrated GH release and are stable throughout the day, were in the upper normal range, so that we can assume the subjects had normal GH secretion. However, it was the aim to investigate whether muscle strength in these athletes could be stimulated further by achieving supraphysiological GH concentrations. With the applied GH doses, IGF-I and its binding protein, IGFBP-3, increased significantly above the normal range. During the trial period we found an equal increase in muscle strength in both groups, GH-treated and placebo. This change has to be considered as an unspecific effect and stresses the importance of the placebo-controlled design of the study. There was no additional effect of GH application on muscular strength or body composition in these highly trained subjects who had no fat stores to be metabolized as potential energy sources. In a similar study the effect of heavy resistance exercise training and additional GH application on muscle size and strength and the rate of whole body protein turnover was examined (6). It was concluded that exercise training increased lean body mass, muscle size and muscle strength, but the addition of GH produced no significant further increase of these parameters. In contrast, in short normal children GH therapy increased growth velocity and deposition of metabolically active tissue, a process which was fuelled by body fat stores (18).

During the course of the trial, GH levels were not suppressed by elevated IGF-I concentrations. Physical exercise may stimulate endogenous GH secretion and it has been suggested that some of the effects of exercise on body composition are mediated by GH (19, 20).

In early animal experiments it has been shown that muscular hypertrophy resulting from treatment with GH did not confer any increase in performance. It was suggested that the material responsible for the increase in muscle weight was not contractile protein (21). Furthermore, in acromegaly the muscles often appear hypertrophied, but are functionally impaired and weaker (22). In contrast, muscle strength improved significantly and was accompanied by changes in body composition in GH-deficient patients after substitution of the hormone (2). In conclusion, our data indicate that the anabolic, lipolytic effect of GH might depend on the degree of fat mass and the GH status. In highly trained athletes with low fat mass, GH treatment had no effect on body composition or physical strength.

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References

10. Blum WF, Ranke MB, Bierich JR. Isolation and partial characterization of six somatomedin-like peptides from human plasma Cohn fraction IV. Acta Endocrinol (Copenh) 1986;111:271–84
11. Ranke MB, Blum WF, Bierich JR. Clinical relevance of serum

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