Effects of Growth Hormone Therapy and Physical Exercise on Anaerobic and Aerobic Power, Body Composition, Lipoprotein Profile in Middle Aged Men

by

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Recently growth hormone therapy has been used as an age delaying drug in middle aged men and women as well as in the elderly. Positive effects have been shown in regards to body mass and body composition changes, fat metabolism, bone mineral density and muscle strength. Exercise is a potent physiological stimulus for growth hormone secretion and both aerobic and resistance exercise results in significant, acute serum increases in GH concentration. It is unclear however whether a combination of exercise and hGH therapy further increases physical performance in adults and increases changes in body composition and biochemical variables related to health. For this purpose a group of 15 middle aged men (45,7±5,8 years, 93,2±16,3kg and 183,3±4cm), slightly overweight were randomly divided into an experimental and control groups. Both groups exercised for 3 month, performing 2 aerobic sessions per week and 2 resistance workouts, increasing training loads every two weeks. The experimental group received additionally hGH subcutaneous injections beginning with 0,2 IU daily for the first month and then increasing it to 0,4 and 0,6 IU in successive month. VO_{2max} was evaluated during a progressive ergocycle test to volitional exhaustion, while anaerobic power and capacity were measured during the 30s Wingate test. Additionally body mass and body composition were evaluated as well as the lipoprotein profile and the concentration of chosen anabolic hormones. The results indicate a significant rise in resting concentrations of GH and IGF-1 after the replacement therapy but no additional benefits in regards to aerobic fitness and fat metabolism in comparison to exercise only. A more profound effect was observed in case of anaerobic performance, thus it was concluded that even small doses of hGH stimulated additional protein synthesis following resistance exercise what allowed for significant increases in FFM, anaerobic power (W/kg) and capacity (J/kg) as evaluated obtained during the Wingate test. It was concluded that for a more significant effect of hGH therapy in regards to physical performance greater doses of this hormone have to be used, along with an intensive exercise program.

Key words: growth hormone, physical performance, body composition, lipoprotein profile

Introduction

Athletes striving for excellence in sports often seek the benefits of pharmacological tools, of which anabolic hormones have been the most popular and effective therapies in the past few decades. More recently growth hormone (hGH) and insulin–like growth factor-1 (IGF-1) injections have become very popular in competitive athletes, attempting to in-

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crease strength, power, muscle mass and decrease fat content (Thorner et al. 1997). Ever since the recombinant human growth hormone is available, it has been used on a wide scale clinically in subjects with growth hormone deficiency (GHD) and to a smaller degree to treat the elderly in case of muscle atrophy, osteopenia, obesity, cardiac dysfunction and other disorders (Cummings et al. 1999, Taaffe et al. 1994). In the last 10-15 years GH therapies have also become popular with the general public as effective anti-aging strategies (Yarasheski et al. 1992, Wallymshmed et al. 1997, Bouillanne et al. 1996).

The acidophilic cells of the anterior pituitary secrete molecules that make up the family of growth hormone (GH) polypeptides. Pituitary GH encoded by the GH-1 gene is secreted in a pulsatile fashion in 6-12 discreet pulses per day. Many physiologic factors alter pulsatile GH secretion, including age, gender, body composition, sleep, nutrition, exercise and serum concentrations of gonadal steroids, insulin and IGF-1 (Giannoulis et al. 2006, Godfrey et al. 2003, Mukherjee et al. 2004).

Human GH represents a family of proteins rather than a single hormone and over 100 forms of GH have been identified in plasma (Baumann 1991). With apparently different physiological functions. In the circulation, GH has a short half-life (20-25min) and the dominant form of GH is a 22kD protein. However, approximately 10% of circulating GH is a 20kD protein and there are also various biologically active lower molecular weight fragments of GH and other protein-bound GH and aggregates of GH (Baumann 1991, Roemmich et al. 1997). GH receptors are found in many tissues throughout the body including skeletal muscle (Lewis et al. 2000).

GH thus has anabolic effects on muscle cells. It acutely stimulates muscle protein synthesis, decreases the rate of glucose use and thereby antagonizes the effects of insulin, promotes the release of free fatty acids and glycerol from adipose tissue, increases circulating free fatty acids and their oxidation in the liver. It also promotes a positive calcium, magnesium and phosphate balance and causes the retention of sodium, potassium and chloride ions (Lewis et al. 2000, Godfrey et al 2003).

Insulin-like growth factor-1 (IGF-1) secreted by hepatic tissue is the primary mediator of the responses regulated by GH in tissues throughout the body including postnatal development of skeletal muscle (Yarasheski 1994). Despite the significant resistance, exercise-induced GH response much of the stimulus for protein synthesis has been attributed to IGF-1. Thus it seems that GH alone may not increase skeletal muscle protein and muscle strength but the combination of GH and IGF-1 can have profound effects on muscular hypertrophy and force development (Yarasheski et al. 1995, Godfrey et al. 2003). GH production and release decreases with age by approximately 14% per decade after the age of 40 and is further decreased in conditions such as obesity. Exercise is a potent stimulus of GH release in young adults, yet it diminishes with age. Since decreased GH secretion in aging and other conditions such as obesity is associated with many detrimental health effects it can be suggested that the use of regular exercise as a stimulator for GH release may have positive health effects. An alternative can be found in hGH therapy and perhaps the greatest health and physical performance benefits can be obtained when growth hormone therapy is combined with a adequate exercise program. This seems especially true for middle aged men and women as well as the elderly (Urhausen et al. 1995).

In general, GH and growth factors promote protein accretion, increase muscle fiber hypertrophy, and improve physical performance. Specifically, the GH/insulin-like growth factor-I (IGF-I) axis is thought to play a pivotal role by serving as a systemic mediator orchestrating nutrient partitioning away from fat deposition and toward protein synthesis, what can be very significant for athletes, especially those were increased lean body mass allows to reach greater relative values of power (sprints, jumps, combat sports, teams sports, gymnastics) (Veldhuis et al. 2004, Verhelst et al. 2002). GH is most popular with body builders and fitness performers, were besides physical performance aesthetic aspects of the body are crucial for success. Many bodybuilders use GH each week during a cycle (e.g., 1-2 IU every other day) to speed up recovery and increase lean body mass (Weltman et al. 2003). In the competitive environment (e.g., bodybuilding), GH is often not used alone, and when it is used with various combinations of synthetic testosterone administrations, a synergistic effect appears to occur (Veldhuis et al. 2005, Rodriguez-Arnao et al. 1999). Thus, while one can examine the effects of GH, the "real world" presents a complex picture of different combinations of anabolic drugs that anecdotally appear to be more effective than single-drug use. However, the desired result of increased mus-

cularity is not without unwanted adverse side effects (Godfrey et al. 2003).

A number of pharmaceutical companies have developed and marketed a multitude of recombinant human growth hormone (rhGH) products with the generic name somatropin.

These rhGH products are typically administered intramuscularly or subcutaneously. The prescribed dose for anti-aging purposes ranges from 0.2 to 0.6 IU administered daily in different cycles for a total period of several weeks up to a year (Svensson et al. 1999). Athletes in strength-power sport disciplines often use doses of 4-6 IU daily and as mentioned before combine GH injections with anabolic steroids to increase the ergogenic effects (Yarasheski 1994). One must emphasize that all recombinantly produced GH products are synthetic versions of the 22-kD GH form. Again, even though this form seems to be the predominant in the human circulation, it is quite possible that there are a number of physiological actions mediated by GH variants that are not accomplished by exogenous administration of the parent 22-kD from of the hormone.

Growth hormone can exert both a transitory insulin-like effect and an anti-insulin diabetogenic effect (i.e., raises circulating glucose). The mechanism for the diabetogenic effect appears to be a reduced peripheral uptake and utilization of glucose. Growth hormone decreases the sensitivity to insulin downstream from the insulin receptor, possibly via reduced synthesis of GLUT 1 (Weltman et al. 2001, 2008).

Growth hormone exerts potent lipolytic effects. The possible mechanisms accounting for these include (1) direct effect, (2) increase in other lipolytic hormones such as catecholamines and glucagons, and (3) influence on adipocyte (i.e., fat cell) responsiveness to other hormones. Growth hormone can directly blunt lipogenesis by decreasing the transcription and synthesis of key lipogenic enzymes:

acetyl-CoA carboxylase, glucose-6-phosphate dehydrogenase, fatty acid synthase, 6-phosphogluconate dehydrogenase, and isocitrate dehydrogenase. Indirectly, GH may increase adrenergic receptor number or reduce inhibitory factors (Lewis et al. 2000, Baumann 1991).

Perhaps the most glamorized effects of GH are on muscle protein synthesis. Growth hormone enhances amino acid uptake and transport, thereby increasing the capacity for protein synthesis. GH optimizes the efficiency and utilization of nitrogen by increasing protein synthesis and decreasing protein degradation. Mechanistically, many of the GH effects on protein are thought to occur indirectly via IGF-I; however, direct effects are also possible. There are many studies which show significant benefits in the above mentioned physiological and biochemical variables as well as physical performance (Monson 2003, Wallymshmed et al. 1997, Lanfranco et al. 2003, Fernholm et al. 2000) and there appears to be an equal amount of studies which do not confirm ergogenic effects of GH therapy. These discrepancies are most likely caused by different research material (age, sex, health status), time of the therapy, doses of GH and the inclusion of exercise program (type, frequency and intensity). The main objective of this research project was to evaluate the combined effects of physical performance and hGH replacement therapy on aerobic and anaerobic fitness, body composition and several health related biochemical markers in slightly obese, middle aged men.

Material and Methods

Subjects

The research material included 15 healthy, middle aged men with an average age of 45,7±5,8 years, slightly overweight. Their basic morphological and

Table 1

Basic morphological and functional characteristic of tested subjects. The variables include: maximal oxygen uptake (VO2max), erythrocyte number (RBC), leukocyte number (WBC), haematocrit value (Ht), hemoglobin concentration (Hb).

Variable	Experimental Group	Control Gprup
Body mass (kg)	95,3±17,8	92,1±16,1
Body height (m)	180.37±3,62	186.23±4,79
VO2max (ml/min/kg)	40,18±6,56	40,40±5,12
RBC (T/L)	4,81±0,3	4,82±0,6
WBC (G/L)	6,44±1,9	5,71±0,9
Ht (L/L)	0,42±0,02	0,43±0,02
Hb (mmol/L)	9,3±0,5	8,9±0,6

functional characteristics are presented in table 1.

Experimental protocol

All of the subjects that volunteered for the research were randomly divided into a experimental group, which exercised for 3 month along with hGH injections and a control group that was submitted only to the exercise program. All of the participants took no medications or supplements one month prior to the beginning of the experiment. The training program was a combination of aerobic and anaerobic exercise, carried out 4 times per week with a systematical progression in training loads every 2 weeks. The subjects performed 2 aerobic sessions per week on a stationary ergocycle, pedaling continuously for 20min at an intensity of 70-75% HRmax. Every 2 weeks the volume of work was increased by 5min, thus during the last part of the experiment they pedaled for 45min in a single training session.

The anaerobic training consisted of general strength exercises performed for the abdomen, back, biceps, chest, forearms as well as the lower limbs. The following exercises were performed in a circuit like manner: bench press, lat pulldown, leg press, hamstring curl, sits ups, upright row, lying leg lifts and the biceps curl. During the first month of the program 3 sets of 8-12 repetitions with 60-70% 1RM were performed, while in the second and third month of the experiment the number of sets was increased to 4 and 5 respectively. The aerobic training sessions were conducted on Monday and Thursday, while strength workouts were carried out on Tuesday and Friday or Saturday if preferred.

The experimental group received additionally hGH subcutaneous injections beginning with 0,2 IU daily for the first month and then increasing the dose to 0,4 and 0,6 IU in successive month.

Physical performance and body composition testing procedures

The experiment had two series of laboratory tests, separated by a three months intervention program , which included physical exercise and hGH injections. The first series of testing was conducted at the beginning of experiment for initial values of analyzed variables. During the first day of testing, before breakfast, resting blood samples were drawn from the antecubical vein to determine biochemical variables. Then, the initial values of body mass (BM) and body composition (fat free mass - FFM, fat con-

tent - Fat%, and total body water - TBW) were evaluated with the use of electrical impedance (Inbody 720, Biospace Co., Japan).

Following, the 30 second Wingate tests were administered to determine anaerobic power and capacity. Before the warm-up, capillary blood samples were drawn to determine resting lactate concentration. The warm-up resistance was set at 100W for 5-min and pedal frequency of approximately 70-80 revolutions per minute. Next, the 30 second Wingate test was preformed with the resistance adjusted to the athlete's body weight (0,08Nm/kg). After the Wingate test, the cool-down resistance was set at 50W for four minutes. All subjects were instructed to cycle as quick and forcefully as possible thought the entire 30s duration of the test. Capillary blood samples were drawn from the finger tip after 4-min of recovery to determine maximal lactate concentration.

The next day, each athlete performed a ramp ergocycle test (T_{20x1}) (20W per 1min) were work load increased linearly (0.33W per 1s) until volitional exhaustion, to establish VO_{2max}. Every ramp test was started with a resistance set at 40W and individual pedal frequency. In this phase, capillary blood samples were drawn to determine lactate concentration before and immediately at the end of the T_{30x1} as well as after the 3rd, 6th, 9th and 12th min of recovery. During the T_{20x1} protocols the following variables were constantly registered: heart rate (HR), minute ventilation (VE), oxygen uptake (VO_2) and expired carbon dioxide (CO_2), respiratory ratio (RER), breath frequency (BF) (MetaLyzer 3B-2R, Cortex).

All tests were performed on an electromagnetically braked ergocycle Excalibur Sport (Lode). Seat and bar height of the cycle ergometer were set according to each subject. Maximal oxygen uptake (VO_2max) was assessed by the attainment of the following criteria: (1) a plateau in VO_2 with increases in work load ($\Delta VO_2 \leq 150$ mL/min at VO_2peak; (2) maximal respiratory exchange ratio (RER) ≥ 1.1. All breath-by-breath gas exchange data were time-averaged using 15 s intervals to examine the oxygen plateau.

Biochemical analysis

Blood samples were drawn from the antecubital vein to sterile test tubes in an amount of 5ml at the beginning and end of the experiment. An anticoagulant (EDTA) was placed in one for the evaluation of blood morphology, while serum was isolated for the second test tube in which the concentration of

insulin (mlU/L) and testosterone (nmol/L), were measured with the with the isotope method in the Automatic Gamma Counter CKR-Wallace device. The insulin-like growth factor 1 (IGF-1) (ng/ml) and human growth hormone (ng/ml) were evaluated with the immunoenzymatic method with the use of a spectrometer ALISA mod. SIR10 S. Additionally the lipoprotein profile was diagnosed [triglycerides (TAG) (mg/dl), total cholesterol (T-Ch) (mg/dl), HDL cholesterol (HDL-Ch) (mg/dl) and LDL cholesterol LDL (LDL-Ch) (mg/dl) with Randox (GB) diagnostic kits with the use of a spectrophotometer UV VIS 1200 Shimadzu. The concentration of LDL-Ch was calculated from the Friedewald formula (mg/dl = T-Ch – TG/5 – HDL-Ch). During the aerobic and an-aerobic exercise test protocols capillary blood sam-ples from the finger tip were drawn to evaluate plasma lactate concentration and acid-base balance. The research project was approved by the Ethics Committee for Scientific Research at the Academy of Physical Education in Katowice, Poland.

Statistics

The results were presented as mean values (x) with standard deviations (SD). The significance of hGH therapy and exercise on aerobic and anaerobic power as well as biochemical variables was performed with the use of ANOVA in a single classification with repeated measures (independent variable - exp. and cont. group). The evaluations were performed twice, initially and after the 3 month intervention which included hGH therapy and exer-cise. The level of statistical significance was set $p < 0.05$.

Results

The lipid profile

The results of ANOVA showed no statistically significant effect of growth hormone administration and increase of physical activity on the management of body fats (tab.2). In case of triglycerides (TAG) the *p value equaled* 0.42 (F=0, 75), for total cholesterol (Ch-T), p=0, 88 (F=0,023), for HDL cholesterol - HDL (HDL-Ch) p=0, 71 (F=0,139) and for LDL cholesterol (LDL-Ch) respectively p=0, 59 (F=0,304) (tab. 2). The greatest effect of hGH administration and exercise was observed in case of TAG, where the concentra-tion of this metabolite decreased after the 3 month experiment by 14,4 %, yet this difference was statisti-cally insignificant, most likely do to a large SD.

The levels of selected hormones

The experiment indicated a significant effect of hGH therapy and exercise on the serum concentra-tion of this hormone p<0,05 with F=8, 46 (fig. 3). Post-hoc analysis showed a significantly higher resting level of this hormone following the experiment p<0,01. The level of hGH after the 3 month experiment was also significant in relation to the control group, which was subjected only to a exer-cise program without the GH replacement therapy p<0,01 (fig. 3). The GH therapy and exercise program included in the 3 month experiment did not change significantly the resting concentrations of IGF-1 (p=0,138 with F=2,52) (fig. 2), testosterone (p=0,53

Table 2

Serum lipid profile in men of the experimental (Group I) and control (Group II) groups, triglycerides (TAG), total cholesterol (Ch-T), cholesterol HDL (HDL-Ch), cholesterol LDL (LDL-Ch)

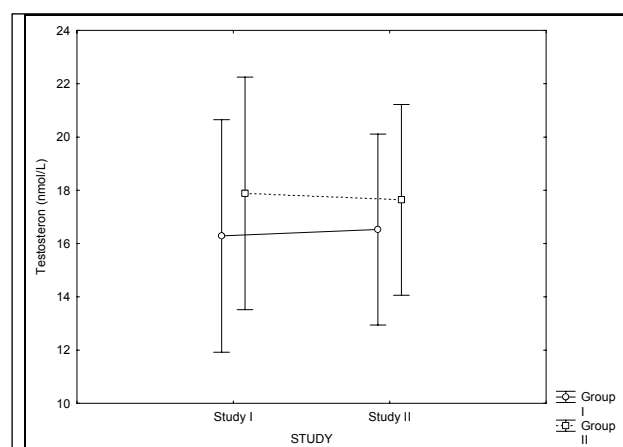| Variables	Groups	Initial (X±SD)	Final (X±SD)
TAG	I	110,9±52,8	95,0±23,8
(mg/dl)	II	124,8±40,9	121,5±33,2
Ch-T	I	203,1±13,3	209,5±16,3
(mg/dl)	II	196,4±26,8	192,4±15,9
HDL-Ch	I	64,8±11,1	70,1±10,5
(mg/dl)	II	68,9±4,3	65,6±4,3
LDL-Ch	I	117,4±9,8	120,4±12,6
(mg/dl)	II	127,6±11,4	128,8±8,7

Figure 1

Serum testosterone concentration of men in the experimental (group I) and control (group II) groups, in initial (study - I) and final study (study - II)
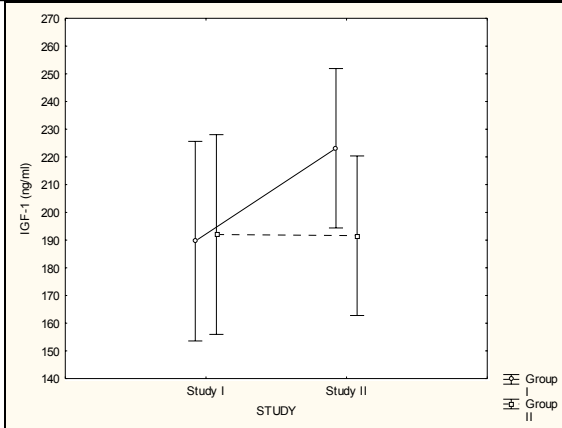
Figure 2

Serum insulin like factor-1 (IGF-1) concentration of men in the experimental (group I) and control (group II) groups. in initial (study - I) and final study (study - II)
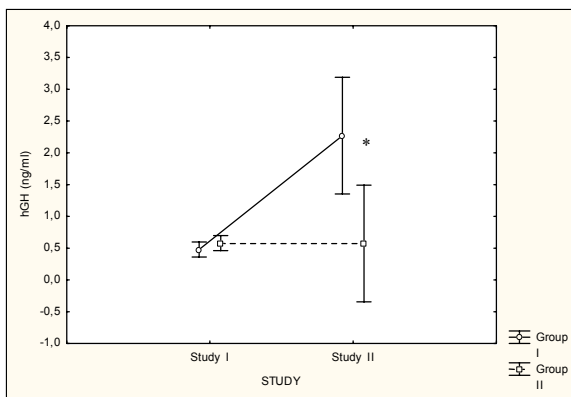

Figure 3

*Serum human growth hormone (hGH) concentration of men in the experimental (group I) and control (group II) groups, in initial (study - I) and final study (study - II),*statistically significant difference at p<0,01*
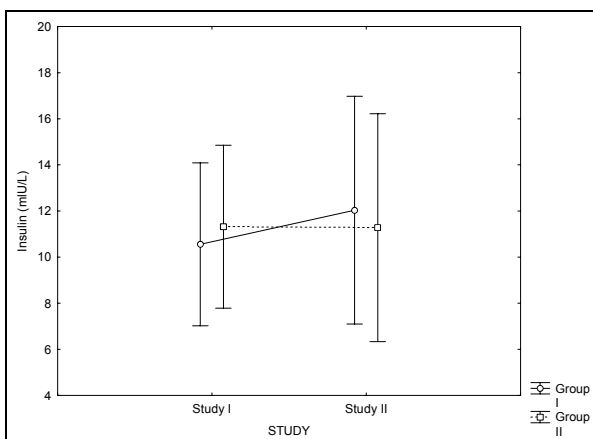

Figure 4

Serum insulin concentration of men in the experimental (group I) and control (group II) groups, in initial (study - I) and final study (study - II)

Table 3

*Aerobic and anaerobic exercise variables: anaerobic threshold expressed in workload (AT - W), anaerobic threshold expressed in heart rate (AT - HR), maximum work load (WRmax - W), relative peak power (Pmax), relative total work (Wt), plasma lactate concentration (LA) (4th min of recovery after the Wingate test), experimental (group I) and control (group II) groups, *statistically significant difference at p<0,01*

Variables	Groups	Initial (X±SD)	Final (X±SD)
AT (W)	I	249,8±42,4	258,8±39,2
	II	257,0±30,6	260,5±31,9
AT (HR-bpm)	I	161,1±10,2	164,0±16,1
	II	160,4±8,6	160,5±9,5
WR max (W)	I	302,9±30,9	309,9±28,9
	II	304,1±33,6	304,6±26,6
P max (W/kg)	I	15,0±2,0	16,5±1,1
	II	14,8±1,6	15,2±1,6
Wt (J/kg)	I	221,8±21,3	233,9±19,6*
	II	227,4±15,8	228,5±13,4
LA (mmol/l)	I	7,8±0,6	8,1±0,7
	II	7,2±0,8	7,5±0,8

with $F=0,001$) (fig.1) and insulin ($p=0,68$ with $F=0,174$) (fig. 4). Figure 2 shows that the applied hGH therapy and exercise program allowed for a large increase in IGF-1, yet once again this difference was statistically insignificant.

Selected physical performance variables

The results of ANOVA with repeated measures did not show a significant effect of hGH injections and exercise on VO_2max ($p=0,18$ i $F=1,98$), yet one must indicate that the increment in aerobic power was greater in the experimental group subjected to the hGH therapy (fig 4). The same was true for values of the anaerobic threshold measured by the obtained workload ($p=0,37$ with $F=0,85$) or heart rate ($p=0,38$, with $F=0,82$), as well as in maximal workload obtained in the test protocol performed to volitional exhaustion ($p=0,37$ with $F=0,84$). The hGH therapy had a significant effect on anaerobic power indices. During the 3 month exercise program peak power ($p<0,05$ with $F=5,42$), total relative work ($p<0,05$ with $F=6,74$) and post exercise lactate concentration were significantly higher in the experimental group ($p<0,05$ with $F=6,15$ (Table 4).

Table 4

Body composition, body mass (BM), fat-free mass (FFM), body fat content in percent (BF), water content (TBW), in experimental (group I) and control (group II) groups

Variables	Groups	Initial (X±SD)	Final (X±SD)
BM (kg)	I	95,3±17,8	92,1±16,1
	II	97,7±8,4	98,1±4,9
FFM (kg)	I	76,8±10,0	78,1±11,2
	II	85,1±8,4	85,2±7,8
BF (%)	I	18,0±9,9	16,8±9,2
	II	20,2±5,7	19,1±6,3
TBW (L)	I	55,8±7,3	55,7±6,6
	II	60,1±9,5	60,6±13,7
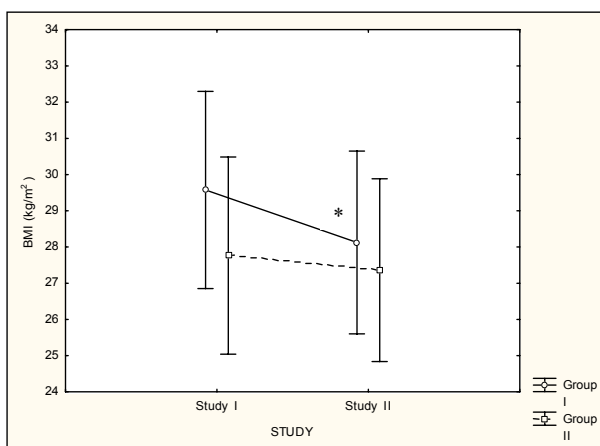
Figure 5

*Body mass index (BMI) in experimental (group I) and control (group II) groups, in initial (study - I) and final study (study - II), *statistically significant difference at p<0,01*

Selected body composition variables

The results of ANOVA indicate no significant effect of hGH injections and exercise on BM (p=0,18 with F=1,96), yet the experimental group showed a tendency to lower this variable quite substantially (tab 5). The hGH therapy also did not influence significantly the level of FFM and TBW (p=0,37 with F=0,84), (p=0,92 with F=0,008) respectively. When body fat was expressed in relative values as % BF the injections of hGH combined with the exercise program showed a significant reduction in this variable (p<0,05 with F=7,85) (tab 5). The same was true for BMI (p<0,01 with F=16,1). The experimental group significantly lowered the values of BMI compared to initial evaluations (p<0,01) (Fig 5).

Discussion

The most important findings of this study indicate that exercise, of both aerobic and anaerobic character is a good stimulus for endogenous growth hormone secretion. The problem seems to be with the intensity of exercise rather than with its nature, as several research projects have indicated that there are lower intensity levels which elicit such effects (Weltman et al. 2008). For example in resistance exercise at training loads between 70-85% 1RM and repetitions performed to failure in the range of 5-12 result in highest GH serum increases (Weltman et al. 2001). Aerobic, continuous exercise has to be performed at intensity of at least 60-70-%VO₂max, at a volume of more than 20-30 min and no less than 2-3 times weekly. The main problems with reaching all or most of these exercise variables is age, where subjects especially over 60 have a difficulty maintaining such intensity. Thus growth hormone therapy in middle aged subjects and the elderly can be an alternative in ant aging strategies and may significantly help in increasing the health benefits of exercise (Lanfranko et al. 2003). Our project showed that adding hGH injections with small doses along to a regular endurance and resistance exercise program in middle aged men brings additional healthy benefits, especially in regards to increased serum GH and IGF-1concentartion, lowered body mass and increased FFM with a concomitant decrease in FM. Aerobic fitness was not effected significantly by the GH therapy but anaerobic power and capacity were improved by the resistance training program and further adaptive changes occurred do to the hGH injections.

The available data on research conducted with GH therapy and related to physical performance is quite controversial, most likely because of the status of the subjects submitted to the exercise program, the type and intensity of exercise, as well as the doses of hGH used and the length of the program. For example in Yarasheski's et al. (1992) first experiment, 16 men were randomly assigned to a resistance-trained group supplemented with GH (40g rhGH/kg/day) or a resistance-trained group supplemented with placebo. Both groups performed a total body resistance training program for 12 weeks. Fat-free mass and total body water increased in both groups, but to a larger extent in the group that received GH. Whole-body protein synthesis and protein balance were higher in the GH group. However, quadriceps muscle protein synthesis rate, torso and

limb circumferences, and muscle strength did not increase to a greater extent in the GH-treated group. Consequently the authors concluded that the large increase in fat-free mass (FFM) with GH treatment was probably attributable to an increase in lean tissue other than skeletal muscle (e.g., connective tissue). Furthermore, resistance training supplemented with GH did not increase muscle hypertrophy or strength better than resistance training alone. The next study Yarasheski et al. (1992) involved experienced weight lifters. Fractional rate of skeletal muscle protein synthesis and the whole-body rate of protein breakdown were determined in seven male weight lifters before and after 14 days of GH administration (40 g rhGH/kg/day).

This study showed that short-term GH treatment did not lead to metabolic adaptations that would augment further increases in muscle mass. Yarasheski et al. (1995) next evaluated the effect of GH administration in conjunction with resistance training in older men. Twenty-three healthy sedentary older men (mean age 67 years) underwent a 16-week progressive resistance training program with GH administration (n = 8) or placebo (n=15). The GH-treated group received 12.5-24 micrograms/kg/day. As with the younger men the GH-treated group experienced greater increases in FFM and total body water than the placebo group. Whole-body protein synthesis and breakdown rates increased in the GH group. However, vastus lateralis muscle protein synthesis rate, urinary creatinine excretion, and training-specific muscle strength were similar in the two groups. As in the study with younger men, Yarasheski et al. (1995) concluded that daily GH treatment does not further augment strength and anabolism associated with a resistance training program. In addition, the increase in FFM was attributed to an increase in noncontractile protein and fluid retention. Taaffe et al. (1994) also researched the effects of rhGH supplementation in conjunction with resistance exercise in older men. Eighteen healthy older men (65-82 years) were trained for 14 weeks to establish a conditioned state. Subjects were then randomized to receive either 0.02 mg/kg body weight/day rhGH or placebo. Subjects then underwent an additional 10 weeks of resistance training. Absolute body mass was not altered in either group; however, changes in body composition were observed, with an increase in FFM and a decrease in fat mass in the GH-supplemented group. No systemic

difference in muscle strength was observed between the two conditions.

In summary, rhGH supplementation combined with resistance training in healthy younger and older men does not appear to augment muscle strength (Yarasheski 1995). The increases in FFM do not appear to b attributable to contractile protein but rather to noncontractile protein, possibly due to fluid retention or connective tissue (Kanaley et al. 1999). Svensson et al. (1999), 24 obese males (18-50 years) with BMI>30kg/m^2 and waist/hip ratio>.95, 25 mg of MK-677 orally with 150 ml of water. Lipoprotein (a) apolipoprotein A and E, total cholesterol, LDL, HDL, serum triglycerides, and lipoprotein lipase activity. Serum lipoprotein did not change. Apolipoprotein A end E changed at 2 weeks but were unchanged at 8 weeks, as were HDL and serum triglycerides. LDL and lipoprotein lipase activity were unchanged. Yarasheski et al. (1995), 23 sedentary, healthy elderly (64-75 years) men with low serum IGF-I levels. Strength training plus subcutaneous injection of placebo (15) or 12.5-24 µg rhGH/kg/day (8) for 7 days/week after each exercise session for 16 weeks. Serum IGF-I and antibodies to rhGH whole-body protein turnover, body composition and anthropometry, and muscle strength. Despite variation in GH dose, anthropometric, muscle strength, and serum IGF-I response to GH were similar. IGF-I remained unchanged in placebo group while increasing two-fold in GH group with increases in fat-free mass (FFM). Taaffe et al. (1994), 18 healthy elderly men (65-82 years), .02mg/kg/day. Muscle strength, body composition, circulating levels of IGF-I, IGFBP-3. IGF-I and IGFBP-3 increased. There was no effect on muscle strength. Body weight did not change, but lean mass increased and fat mass decreased. Yarasheski et al. (1992), 16 young healthy untrained men (27 years). Strength training plus subcutaneous injection of placebo (9) or 40 µg rhGH/kg/day (7) after each exercise session, 5 days/week for 12 weeks. GH, IGF-I, OGTT, insulin levels, body composition and anthropometry, muscle strength, whole-body protein turnover, and muscle biopsy. Serum GH curve and serum IGF-I remained unchanged in placebo, while GH curve in treated subjects increased. Glucose and insulin were unaffected by training or treatment. Body weight and FFM increased in both groups, but the increment of FFM was greater in the GH-treated group.

It was concluded that for a more significant effect of hGH therapy in regards to physical performance

greater doses of this hormone have to be used, along
with an intensive exercise program.

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