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Original Research Paper

EFFECACY OF GROWTH HORMONE THERAPY IN POSTMENOPAUSAL OBESE FEMALES

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ABSTRACT

Background: Growth hormone (GH) secretion is decreased in females with abdominal obesity, and this is accompanied by changed cardiovascular risk factors that result in metabolic syndrome. When GH was administered to females with abdominal obesity, their metabolic processes improved; however, there is insufficient information for females.

Aim: to analyze the effects of GH medication on visceral fat mass and glucose tolerance in postmenopausal females with abdominal obesity. It also assesses the effect of GH treatment on lowering abdominal visceral fat.

Methods: A total of 38 postmenopausal females were split into two groups at random, with one receiving placebo treatment and the other receiving growth hormone therapy. Results were derived from assessments of body parameters, insulin sensitivity, and glucose tolerance that were done at baseline (the beginning of treatment), six months, and twelve months after therapy.

Results: At six months, group II's serum levels of IGF-1 increased from 101±6.8 at baseline to 211±15.8 (p~0.001), whereas group I showed no statistically significant change from 121±4.8 to 119±5.8g/L. However, neither group showed a statistically significant difference from six to twelve months. After receiving GH treatment, group II's total triglycerides and HDL cholesterol increased after six months. After receiving GH treatment, visceral adipose tissue dramatically decreased in Group II, going from 177.0±8.5 to 170.4±9.8, while Group I had an increase, going from 161.1±7.7 to 172.0±8.7 (p=0.002).

Conclusion: The current study concludes that growth hormone therapy improves insulin sensitivity, lowers hepatic fat levels, and improves other metabolic syndrome characteristics in postmenopausal females with abdominal obesity.

Keywords: Growth Hormone, Metabolic Disorders, Postmenopause, Abdominal Obesity, Visceral Fat

INTRODUCTION

Abdominal obesity is a powerful and significant risk factor that contributes to the development of Type 2 diabetes mellitus and cardiovascular disease. Type 2 diabetes is linked to insulin resistance, hypertension, and/or dyslipidemia, which together constitute the metabolic syndrome. Insulin resistance is used as the etiologic factor for metabolic syndrome, according to the World Health Organization (WHO).[1] However, the National Health and Nutrition Examination Survey of 1999–2000 (NHANES III) and the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) both list abdominal obesity as a risk factor for metabolic syndrome. Additionally, insulin resistance, atherogenic dyslipidemia, a prothrombotic or proinflammatory condition, and/or prothrombotic state are associated with abdominal obesity.2

Previous evidence has indicated a global increase in metabolic syndrome, regardless of the diagnostic criteria employed. Previous research indicated that men had a higher metabolic prevalence than females. On the other hand, current research indicates that both genders have an equal prevalence of type 2 diabetes mellitus and an equal risk of developing the disease. According to a Framingham Heart study, females with metabolic syndrome had a higher chance of developing cardiovascular disease than men do. There is less evidence for these conclusions, and no other study has supported them.3

In addition to diabetes and heart disease, metabolic syndrome is linked to non-alcoholic fatty liver disease, which can manifest in a variety of ways, from steatosis to steatohepatitis. These conditions are closely linked to hypertriglyceridemia, type 2 diabetes, and/or insulin resistance.

Although the exact pathophysiology of visceral fat deposition in metabolic syndrome is unknown, it is thought to be the result of a number of cumulative endocrine disruptions and changes that impact the gonadal, somatotropic, and hypothalamic-adrenal axes as well as the sympathetic nervous system.4

Adults with growth hormone insufficiency and those with metabolic syndrome have certain characteristics, such as low blood HDL cholesterol, high serum triglycerides, insulin resistance, and increased belly fat. In adults with abdominal obesity, there is a robust and negative relationship between the quantity of visceral adipose tissue and decreased GH secretion. This relationship holds true for both males and females.5. When growth hormone is replaced by exogenous therapy, the lipid profile is improved, the risk of cardiovascular disease is lowered, and visceral fat is reduced. Additionally, after receiving growth hormone replacement therapy for nine months, male patients with abdominal obesity showed improvements in their insulin sensitivity.

Additionally, postmenopausal females who received a 12-week course of growth hormone treatment in addition to exercise and diet had a drop in truncal fat, which is comparable to the effects of exercise and diet. In contrast, obese females who received a 5-week course of growth hormone treatment saw a decrease in body fat mass. Nevertheless, as no research has demonstrated that growth hormone treatment is more effective than weight loss in reducing total body fat in simple obese females, there are no long-term statistics on the effect of GH on abdominal obese females.Six Therefore, the current study was carried out to assess the effects of growth hormone therapy on visceral fat mass and glucose tolerance as well as the reduction of abdominal visceral fat and insulin sensitivity in postmenopausal females with abdominal obesity.

MATERIALS AND METHODS

The current investigation was carried out as a randomized, placebo-controlled trial with approval from the relevant ethical committee. A total of 38 postmenopausal females with a mean age of 57.4 years who were between the ages of 50 and 56 were included in the study. The postmenopausal females who visited the Department of Obstetrics & Gynecology, Chandulal Chandrakar Memorial Government. Medical College, Kachandur, Durg, Chhattisgarh were the enrolled in the study.

Obese postmenopausal females aged 50–70 years, serum IGF-1 levels between -1 and -2 standard deviations, a waist–to-hip (W/H) ratio and/or a sagittal diameter more than 0.85 and 21.0 cm, respectively, and a body mass index (BMI) in the range of 25–35 kg/m2 were the inclusion criteria for the study. Subjects with diabetes mellitus, stroke, heart disease, hormone therapy, including estrogen replacement therapy, intermittent claudicatio, and cancer were excluded from the study. After reviewing the exclusion and inclusion criteria, 38 of the 160 females who had been tested overall were eventually included.

Following final inclusion, 38 trial participants were split into two groups at random, with one receiving placebo therapy and the other receiving growth hormone therapy. The process of randomization was tossing a coin. Before retiring to bed, the growth hormone group received treatment with GH. The first dose was 0.13 mg/day, which was increased to 0.27 mg/day after two weeks, 0.4 mg/day after four weeks, 0.53 mg/day after five weeks, and 0.67 mg/day after six weeks.

At every appointment, any negative effects, symptoms, and indicators were noted. The GH dosage was halved for fluid-related adverse effects. All subjects received both written and verbal instructions at each session. The proportion of vials needed for treatment was expressed by counting the number of empty vials that were returned in order to assess treatment compliance.

Body parameters, insulin sensitivity, and glucose tolerance were measured at baseline (the beginning of treatment), six months, and twelve months following therapy. Only baseline and 12-month CT (Computed Tomography) scans of the belly and thighs were performed, along with quality of life and physical activity assessments. Physical and laboratory examinations were carried out after one month, two months, three months, six months, twelve months, and one month following the end of treatment.

Total body potassium, fat-free mass, and total body fat were measured in relation to body composition. CT was used to quantify the adipose tissues and muscle of the abdomen and thighs. The mid-thigh area, the fourth lumbar vertebra, the mid-liver level, and the fourth cervical vertebra level were all scanned four times. A biochemical method was also used to assess the hepatic fat content; fatty liver was extracted at a threshold of 30/less liver attenuation. The sensitivity to insulin was also evaluated. Oral glucose tolerance test (OGTT) was performed at baseline, six months, twelve months, and one month following the end of medication. IGF-1, triglycerides, serum insulin, blood glucose, and serum total cholesterol were measured from the drawn blood samples.

The statistical analysis of the gathered data was conducted using the ANOVA and t-test functions of SPSS software, version 21.0, 2012, Armonk, NY. The formulation of the results was done with a p~0.05 level of significance.

RESULTS

The mean age of study subjects for groups I and II was 56.42 and 58.28, respectively, and their BMI was 30.2±0.6 and 30.8±0.5, respectively, as shown in Table 1. The two groups were matched with respect to demographic characteristics at the baseline for mean age, BMI, alcohol intake, smoking history, and hypertensive status. All of these characteristics showed a non-significant difference between them.

Additionally, the study groups matched well at baseline in terms of waist, weight, free fat mass, total body fat, waist-hip ratio, sagittal diameter, mean liver attenuation, visceral adipose tissue area, abdominal adipose tissue area, and thigh muscle area; all non-significant differences were indicated by the corresponding p-values of 0.6, 0.8, 0.8, 0.2, 0.7, 0.5, 0.02, 0.7, and 0.02 (Table 2).

At 12 months, Group II received a growth hormone dose of 0.50±0.03 while Group I received a dose of 0.62±0.01, indicating a statistically significant difference (p=0.001). Group II's serum levels of IGF-1 increased from 101±6.8 at baseline to 211±15.8 (p~0.001) at 6 months, while group I had a non-significant shift from 121±4.8 to 119±5.8g/L. From 6 to 12 months, neither group showed a statistically significant difference (Table 3).

Regarding observed complications, at 4 weeks into therapy, 9 females in Group II (GH) experienced mild to moderate fluid retentive side effects; in 1 subject, the symptoms resolved on their own after 8 weeks, while in the remaining 8 females, the symptoms disappeared after

the dose was halved. Two female participants in group I experienced similar effects, which again decreased with dose modifications.

There was no statistically significant difference in the two groups' glucose disposal rates (GDR) at baseline, and there was no significant difference between them after 12 months (p=0.2). According to intragroup analysis, Group II's GDR increased at 12 months and differed statistically significantly from Group I's baseline.

Table 3 indicates that there were no significant alterations observed in the 2-hour glucose values or fasting plasma glucose levels in either group (=0.8 and 0.5, respectively). In terms of lipid and cholesterol metabolism, from baseline to 6 months to 12 months, Group II's LDL cholesterol and total cholesterol levels were lower (4.31±0.14 to 3.85±0.16) than Group I's (4.37±0.22 to 4.27±0.18). After receiving GH treatment, group II's total triglycerides and HDL cholesterol increased after six months. Following GH therapy or placebo, apo lipoprotein A/B (g/L) did not change between the two groups (Table 4).

Between the baseline and 12-month marks, both Group I and Group II's bodyweight increased. Of the participants in both Groups, 10 and 14, respectively, gained more than 1 kg of weight; a p-value of 0.8 indicated that there was no statistically significant difference between the groups. Group I and II had baseline total body fat values of 46.7±1.1 and 48.5±1.1, respectively. There was no intergroup difference in either group's total body fat or free fat mass at any recall period (p=0.8). Likewise, no statistically significant variation was observed in the thigh muscles and abdominal adipose tissue across the groups (p=0.002 and 0.7, respectively). After GH treatment, visceral adipose tissue in Group II dramatically decreased from 177.0±8.5 to 170.4±9.8, while in Group I it increased from 161.1±7.7 to 172.0±8.7 (p=0.002). Quality of life was also the same for both groups.

DISCUSSION

At baseline, the two groups' demographic characteristics were matched with respect to mean age, BMI, alcohol intake, smoking history, and hypertensive status. There was a non-significant difference observed between all characteristics regarding the mentioned demographics; group I's mean age was 56.42, while group II's was 58.28. The study subjects' BMIs were 30.2±0.6 and 30.8±0.5, respectively. With the corresponding p-values of 0.6, 0.8, 0.8, 0.2, 0.7, 0.5, 0.02, 0.7, and 0.02 indicating all non-significant differences, the study groups were also well matched at baseline for waist, weight, free fat mass, total body fat, waist-hip ratio, sagittal diameter, Mean Liver Attenuation, Visceral adipose tissue area, Abdominal adipose tissue area, and Thigh muscle area.

These demographics were comparable to those reported by writers in Taaffe DR et al. (2007) and Tomlinson JW et al. (2008) in 2004. Group II had a rise in serum levels of IGF-1 from 101±6.8 at baseline to 211±15.8 (p~0.001) at 6 months. In contrast, group I experienced a non-significant shift in serum levels from 121±4.8 to 119±5.8g/L, and neither group showed a statistically significant difference from 6 to 12 months. There was no statistically significant difference in the two groups' glucose disposal rates (GDR) at baseline, and there was no significant difference between them after 12 months (p=0.2). According to intragroup analysis, Group II's GDR increased at 12 months and differed statistically significantly from Group I's baseline.

Additionally, there were no discernible increases in either group's 2-hour glucose values or fasting plasma glucose levels (=0.8 and 0.5, respectively). These findings were consistent with those of Nam SY et al. (2001) and Ferrara CM et al. (2002a, 2002), whose results were similar to those of the current investigation.

In terms of lipid and cholesterol metabolism, from baseline to 6 months to 12 months, Group II's LDL cholesterol and total cholesterol levels were lower (4.31±0.14 to 3.85±0.16) than

Group I's (4.37±0.22 to 4.27±0.18). After receiving GH treatment, group II's total triglycerides and HDL cholesterol increased after six months. After GH treatment or a placebo, there was no difference in the levels of apo lipoprotein A/B (g/L) in either group.

Between the baseline and 12-month marks, both Group I and Group II's bodyweight increased. Of the participants in both Groups, 10 and 14, respectively, gained more than 1 kg of weight; a p-value of 0.8 indicated that there was no statistically significant difference between the groups. Group I and II had baseline total body fat values of 46.7±1.1 and 48.5±1.1, respectively. There was no intergroup difference in either group's total body fat or free fat mass at any recall period (p=0.8). Likewise, no statistically significant variation was observed in the thigh muscles and abdominal adipose tissue across the groups (p=0.002 and 0.7, respectively). After GH treatment, visceral adipose tissue in Group II dramatically decreased from 177.0±8.5 to 170.4±9.8, while in Group I it increased from 161.1±7.7 to 172.0±8.7 (p=0.002).

Quality of life was also the same for both groups. These results were similar to the results of Johanson EH et al[11] in 2003 and Sesmilo G et al[12] in 2000 where similar results concerning body fat, free fat mass, and lipid profile were described by the authors.

CONCLUSION

Within its limitations, the present study concludes that growth hormone therapy is beneficial in postmenopausal subjects with abdominal obesity resulting in improved insulin sensitivity, decreased hepatic fat levels, and other metabolic syndrome features. This might result in decreased risk for cardiovascular diseases. However, the present study had few limitations including smaller sample size, shorter monitoring period, geographical area biases, and single-institutional nature. Hence, further longitudinal studies with a larger sample size and longer monitoring period are required to reach a definitive conclusion.

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TABLES

Characteristics	Group I % (n)	Group II % (n)
Total number	19	19
Mean age (years)	56.42	58.28
Smoking		
Positive	21.05 (4)	21.05 (4)
Negative	78.94 (15)	78.94 (15)
Alcohol		
Positive	100 (19)	100 (19)
Negative	0	0
Hypertension	15.78 (3)	15.78 (3)
BMI (kg/m^2)	30.2±0.6	30.8±0.5

Table 1: Demographic characteristics of the study subjects

Characteristics	Group I (Mean±S.D)			Group II (Mean±S.D)			p-value
	Baseline	6 months	12 months	Baseline	6 months	12months	
Waist (cm)	102.04±1.4	102.04±1.6	102.04±1.8	104±1.3	103±1.4	104±1.5	0.6
Weight (kg)	80.7±2.0	80.5±2.1	81.6±2.1	86.0±2.2	86.1±2.4	87.0±2.3	0.8
Free fat mass (kg)	46.7±1.1	47.4±1.1	46.6±1.2	48.5±1.1	48.7±1.1	48.0±1.1	0.8
Total Body Fat (kg)	34.0±1.6	33.0±1.6	35.0±1.5	37.2±1.7	37.1±1.9	38.7±1.8	0.8
Waist: Hip ratio	0.92±0.010	0.92±0.01	0.91±0.01	0.91±0.01	0.90±0.01	0.91±0.01	0.2
Sagittal diameter (cm)	25.0±0.43	24.6±0.46	24.9±0.54	25.6±0.32	25.2±0.41	25.5±0.38	0.7
Mean Liver Attenuation	51.0±2.7	-	51.2±2.3	49.0±2.1	-	51.1±2.0	0.5
Visceral adipose tissue area (cm^2)	161.1±7.7	-	172.0±8.7	177.0±8.5	-	170.4±9.8	0.002
Abdominal adipose tissue area (cm^2)	400.7±20.6	-	400.2±21.8	430.2±22.0	-	432±22.1	0.7
Thigh muscle area (cm^2)	110.7±3.2	-	110.5±3.0	110.2±2.5	-	113.0±2.3	0.002

Table 2: Body diameter and anthropometric characteristics of the study subjects

Characteristics	Group I (Mean±S.D)			Group II (Mean±S.D)			p-value
	Baseline	6 months	12 months	Baseline	6 months	12months	
Glucose Disposal rate (mg/kg min)	7.76±0.46	7.79±0.49	8.07±0.52	8.25±0.55	7.45±0.43	8.55±0.54	0.2
Fasting Insulin (mU/lit)	9.5±0.8	9.8±0.8	10.2±0.7	9.9±0.8	12.6±1.4	13.5±1.1	0.5
2h Glucose (mmol/min)	5.7±0.1	6.9±0.2	6.4±0.2	6.1±0.1	7.2±0.3	6.9±0.2	0.8
Fasting Glucose (mmol/min)	5.0±0.1	5.2±0.1	5.2±0.1	5.0±0.1	5.1±0.1	5.3±0.1	0.2
IGF-1 (µg/liter)	121±4.8	119±5.8	120±6.8	101±6.8	211±15.8	206±18.8	<0.001

Table 3: Insulin and Glucose parameters assessment in the study subjects

Parameter	Group I (Mean±S.D)			Group II (Mean±S.D)			p-value
	Baseline	6 months	12 months	Baseline	6 months	12months	
Apo lipoprotein A/B (g/L)	0.6±0.03	0.7±0.04	0.6±0.03	0.6±0.01	0.6±0.02	0.6±0.02	0.3
Lipoprotein (g/L)	0.40±0.05	0.41±0.05	0.40±0.05	0.26±0.02	0.28±0.03	0.28±0.03	0.6
Triglycerides (mmol/L)	1.47±0.08	1.72±0.22	1.59±0.12	1.47±0.10	1.69±0.17	1.53±0.13	0.7
HDL cholesterol (mmol/L)	1.25±0.06	1.22±0.06	1.25±0.05	1.29±0.04	1.21±0.04	1.29±0.03	0.5
LDL cholesterol (mmol/L)	4.37±0.22	4.27±0.18	4.19±0.21	4.31±0.14	3.85±0.16	4.11±0.15	<0.05
Total cholesterol (mmol/L)	6.32±0.24	6.28±0.21	6.19±0.22	6.29±0.13	5.80±0.16	6.07±0.14	0.05

Table 4: Cholesterol, Lipoprotein, and Apolipoprotein assessment in the study subjects