

CLINICAL INVESTIGATION

Effects of Weight Loss Induced By Eight-Week Orlistat Therapy on Maximal Work Production Capacity in Obese Females

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Abstract: The aim of this study was to examine the effects of weight loss induced by pharmacotherapy combined with a hypocaloric diet for a period of 8-weeks on maximal work (W_{max}) production capacity and aerobic fitness in obese patients. Twelve obese females were put on an integrated energy restricted diet with orlistat supplement 3 x 120 mg/day. Each patient performed 3 incremental ramp exercise tests using an electromagnetically braked cycle ergometer: one at onset, one at the end of 4-weeks and one at the end of the 8-weeks to determine W_{max} production capacity. The first 4-week therapy period resulted in a significant reduction in total body weight (91.4 ± 3.1 kg vs. 88.2 ± 2.9 kg, P = 0.0001) and body fat mass (38.7 ± 1.9 kg vs. 37.5 ± 2.0 kg, P = 0.03). However, the weight reduction achieved during first 4-weeks was not associate with increased W_{max} production capacity: 90.8 ± 5 W vs. 92.9 ± 5 W (P = 0.5). During the 8-week therapy period, further reductions in both body weight (86.0 ± 2.8 kg, P = 0.0001) and body fat mass (36.2 ± 1.8 kg, P = 0.002) were observed. W_{max} production capacity increased slightly but was not statistically significant: 100.4 ± 6 W (P = 0.08). The impaired aerobic fitness of obese patients did not improve during the short-term obesity therapy despite significant decreases in body weight and fat mass. Thus, it is important to consider an aerobic exercise training program known to increase aerobic fitness and W_{max} capacity in addition to short-term dieting and pharmacotherapy.

Key Words: Obesity, orlistat, body mass index, weight loss.

Introduction

Obesity, which describes the condition of an abnormal accumulation of body fat mass, is directly related to increased risk of several chronic diseases, including glucose intolerance, hypertension, hyperlipidemia, hemostatic variables and increased insulin resistance (1,2). Increased positive energy due to the disrupted energy intake and energy consumption balance (3) results in an increased body fat mass.

A caloric restricted diet and increased physical activity can provide a negative energy balance, which is the main target to achieve in obesity treatment. In addition, pharmacological agents have also been widely considered an effective method to provide negative energy balance in obesity treatment. It has been shown that a modest body weight loss (in the order of 5-10% of initial body weight)

as a result of obesity treatment is generally associated with reduced obesity related risk factors (4).

Orlistat (Xenical™) is a pharmacological agent promoting weight loss in obese subjects via inhibiting the pancreatic lipase enzyme (5). The specific effects of long-term orlistat therapy on body weight and body composition have been shown in previous studies (6,7).

However, it should be pointed out that a progressive reduction in cardiopulmonary fitness is one of the biggest problems in obesity (8,9). It is likely to lead serious limitations in the ability of obese patients to perform basic daily activities (10). There are reports suggesting that unfit subjects have a higher risk of illness and death compared to fit subjects with a similar body mass index (8). That is, low levels of physical activity and decreased physical fitness have been shown to be associated with a

marked increase in all causes of mortality (8). In contrast, improvement in cardiopulmonary fitness is also reported to be associated with enhanced survival in patients with obesity (9). Thus, the fitness of obese patients seems to be an important protective factor against the influence of risk factors for mortality (8). Therefore, increasing cardiopulmonary fitness presents an important target in addition to reducing total body weight in obesity treatment. Thus, increased physical fitness becomes an important part of obesity treatment in addition to reducing body weight. In the present study, we examined the effects of weight loss induced by orlistat therapy combined with a hypocaloric diet on body composition, maximal exercise performance and aerobic fitness in obese patients.

Materials and Methods

Twelve sedentary obese females (age: 38.0 ± 2.2 years, height: 158.7 ± 1.8 cm, body mass index: 36.3 ± 1.1 kg/m²) who attended our Obesity Clinic for obesity treatment participated in the study. All subjects had a body mass index above 30 kg/m². Table presents the mean (\pm SE) values of the patients' body compositions before and after the 8-week therapy period.

Before the start of study, all subjects underwent a pre-participation medical exam, including screening for normal glucose tolerance, hormonal analyses (for Cushing disease and/or hypothyroid etc.), plasma lipid profile and ECG for cardiovascular risk assessment. Furthermore, they were also screened for taking any medications known to affect body composition or physical activity. Each patient accepted the risks of the experimental procedure explained to them and signed an informed consent. The test procedures were approved by the Institutional Review Board for the Use of Human Subjects at Firat University in Elazığ in the Department of Endocrinology and Metabolic Diseases.

Anthropometric measurements, including height and weight, were obtained from each subject. During the study, body weight, body mass index and body composition were assessed at least once per week between 0800 and 1000 hours using the leg-to-leg bioelectrical impedance method (Tanita Body Fat Analyser, model TBF 300), which provides an accurate assessment of fat free mass in obese subjects and changes in fat mass with diet (11).

All obese patients had energy restrictions with a hypocaloric diet coupled to drug therapy (orlistat 3 x 120 mg/day) at the optimal dosage (12). The energy content of the diet given to the obese subjects (hypocaloric diet) was 1200-1600 kcal/day (generally, 1400 kcal/day).

The patients were fasted overnight (no eating or drinking) and were also requested to refrain from taking drugs, or caffeine for a period of 12 h before the test. After becoming familiar with the testing equipment, a symptom limited maximal exercise test was performed by each subject to assess cardiopulmonary and metabolic functional capacity.

Each patient performed 3 incremental ramp tests protocol as described by Whipp et al. (13) at a work rate of 15 W/min using an electromagnetically braked cycle ergometer (LODE, Groningen, The Netherlands): one on the first day of the study, the second after 4-weeks and the last after 8-weeks of therapy.

The exercise test protocol consists of 3 phases: initially, the subjects started pedalling for 4 min at a power of 20 W (60 rpm) as a warm-up period, then incremental period where the work rate was increased 15 W/min with a work rate controller until the subjects could no longer continue to maintain the work rate and lastly recovery period where the cycle ergometer power was reduced abruptly again to 20 W and the subjects continued to cycle for 4 min.

Throughout the test, the subjects had to wear a 6-lead heart rate monitor to follow ECG and heart beat. A paired t test was used to evaluate the statistical significance of differences between basal, 4-week and 8-week values. Differences were considered significant at $P < 0.05$.

Results

The individual values for the percentage changes in body weight, fat mass, and fat free mass after 4 and 8-weeks of progressive supervised therapy with hypocaloric diet and orlistat are shown in Figure 1.

During the study, there were significant reductions in body weight [91.4 ± 3.1 kg (basal) vs. 88.2 ± 13.5 kg (4-weeks, -3.5%, $P = 0.0001$) and 86.0 ± 2.8 kg (8-weeks -5.9%, $P = 0.0001$)] and in body fat mass [38.7 ± 1.9 kg (basal) vs. 37.5 ± 1.1 kg (4-weeks, -3.1%, $P = 0.03$) and 36.2 ± 1.8 kg (8-weeks, -6.4%, $P = 0.002$)]

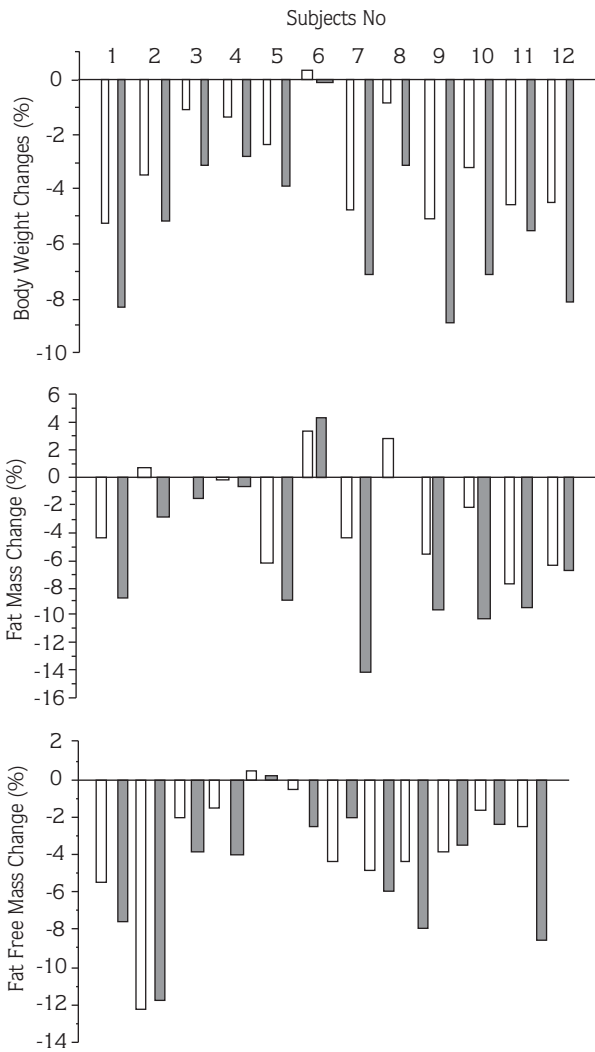


Figure 1. The changes in individual values for the total body weight, fat mass, fat free mass in response to 4 (white column) and 8-weeks (dark column) of dieting and orlistat therapy. These values reflect the percentage of differences between basal vs. 4-week (white column) and basal vs. 8-week (dark column) therapy periods.

(Table). In addition, fat free mass also decreased significantly [53.0 ± 1.7 kg (basal) vs. 50.6 ± 1.1 kg (4-weeks, -4.5% , $P = 0.005$) and 49.8 ± 1.1 kg (8-weeks, -6.0% , $P = 0.001$)] (Table).

Body weight reduction during the first 4-weeks of therapy did not have a significant effect on patients' Wmax production capacities (Table, Figure 2). The Wmax was 90.8 ± 5 W at basal and 92.9 ± 5 W at 4-weeks ($P = 0.5$). Furthermore, at the end of the 8-week period, there was a small statistically insignificant increase in Wmax production capacity (100.4 ± 6 W, 10.5% , $P = 0.08$) (Table).

During the study period, Wmax production capacity with regard to each kilogram of body weight was 1.008 ± 0.06 W/kg (basal) to 1.069 ± 0.06 W/kg (4-weeks, $P = 0.1$) and 1.180 ± 0.07 W/kg (8-weeks, $P = 0.01$) (Table, Figure 3).

As can be seen in Figure 4, a linear correlation between Wmax production capacity with regard to each kilogram of body weight and body mass index was found [$R = -0.519$, (basal, $P = 0.08$), $R = -0.723$, (4-weeks, $P = 0.007$); $R = -0.721$, (8-weeks, $P = 0.008$)].

Discussion

It is known that a low level of physical activity can significantly and independently contribute to obesity. As expected, obese patients' Wmax production was found to be lower than that of normal subjects (14). Reduced aerobic fitness and exercise capacity are closely related with the level of cardiopulmonary fitness and these findings are commonly observed in patients with a high body mass index (15). Reduced aerobic fitness expressed as decreased Wmax production capacity is an important

Table. The mean (\pm SE) values and ranges for body mass index (BMI), body weight, fat mass (FM), fat free mass (FFM), maximal work rate production (Wmax) and maximal work rate production capacity with regard to body weight (Wmax/BW at the onset of the study (basal) and at the end of the 4 and 8-week therapy periods with dieting and orlistat.

	Basal	Four-week period (% change from the basal)		Eight-week period (% change from the basal)	
BMI (kg/m ²)	36.3 ± 1.1	$35.0 \pm 1.0^*$	-3.5%	$34.1 \pm 0.9^*$	-6.0%
Weight (kg)	91.4 ± 3.1	$88.2 \pm 2.9^*$	-3.5%	$86.0 \pm 2.8^*$	-5.9%
FM (kg)	38.7 ± 1.9	$37.5 \pm 2.0^*$	-3.1%	$36.2 \pm 1.8^*$	-6.4%
FFM (kg)	53.0 ± 1.7	$50.6 \pm 1.1^*$	-4.5%	$49.8 \pm 1.0^*$	-6.0%
Wmax (W)	90.8 ± 5	92.9 ± 5^{NS}	2.3%	100.4 ± 6^{NS}	10.5%
Wmax/BW (W/kg)	1.008 ± 0.06	1.069 ± 0.06^{NS}	6.0%	$1.180 \pm 0.07^*$	17%

*Indicates statistically significant differences compared to basal values

NS: not significant

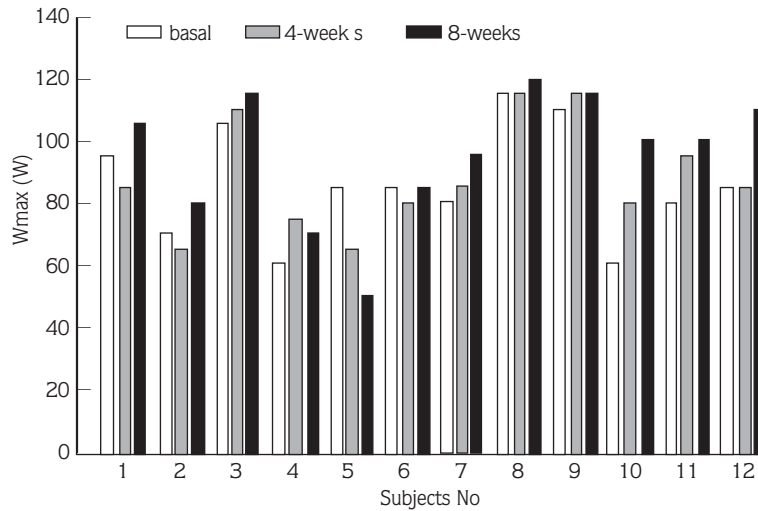


Figure 2. The obese patients' maximal work production (Wmax) capacities at the onset of the study (white column) and at the end of the 4 (grey column) and 8-week (black column) therapy periods.

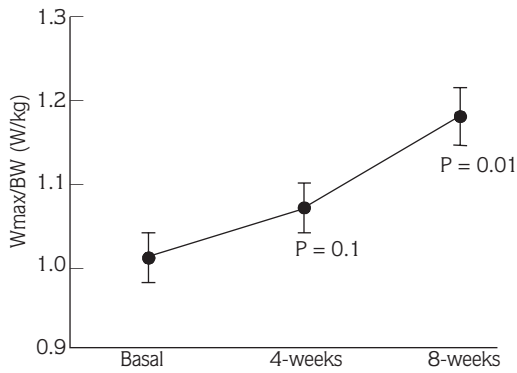


Figure 3. The mean (\pm SE) values for maximal work production capacity with regard to the to the body weight (Wmax/BW) at the onset of the study (basal), at the end of the 4-week and 8-week therapy periods.

factor affecting energy intake to the ratio of consumption and leading to a positive energy balance and excess fat mass (16,17). It has been shown that Wmax capacity with regard to the body weight ratio can be useful in the determination of work capacity and also aerobic fitness when the measurement of O_2 uptake is not available (18,19). The determination of Wmax production capacity through incremental exercise testing has been used as an important indicator of cardiopulmonary fitness in subjects of different fitness levels.

A systematically reduced exercise capacity can be linked to reduced O_2 supply to the muscles during activity.

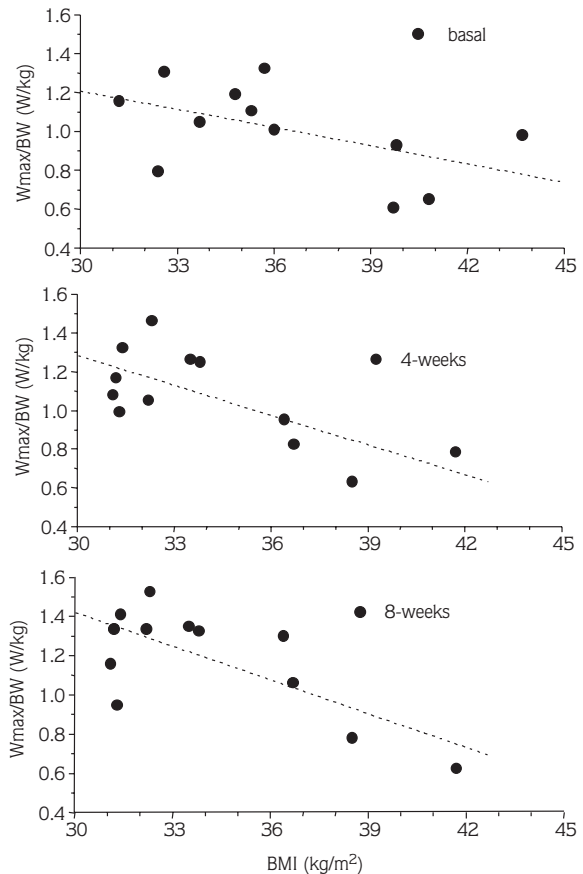


Figure 4. The correlation between maximal work production capacity with regard to body weight (Wmax/BW) and body mass index (BMI) at the onset of the study (basal), and at the end of the 4 and 8-week therapy periods.

An increase in type II muscle fibers and a decrease in type I muscle fibers (20) as well as cardiovascular (21) and pulmonary factors (22) may have an important effect on the reduced work capacity of obese patients.

Analysis of our data showed that 4-week orlistat and diet therapy produced a significant decrease in body weight and fat mass reduction in our study group (23). However, as can be seen in Figure 1, body weight loss and fat mass reduction varied widely among the subjects. This result shows the importance of a subject's response to obesity therapy consisting of dieting and orlistat. Despite significant reductions in total body weight and fat mass after 4-weeks of therapy, aerobic fitness as indicated by Wmax production capacity did not increase (24). Similarly, Wmax for each kilogram of body weight after 4-weeks did not improve significantly.

In obesity treatment, reducing body weight without improving aerobic fitness and work production capacity may not benefit patients. Previous studies have shown that weight loss results in a decrease in resting metabolic rate and an increase in the respiratory quotient (i.e. shift in substrate utilization from fat to carbohydrates) (25,26). Importantly, a reduced resting metabolic rate and an increased respiratory quotient can result in a greater risk of body weight gain (27,28).

After 8-weeks of therapy, despite the observation of further reductions in total body weight and fat mass, there was no significant improvement in Wmax production capacity ($P = 0.08$). Wmax for each kilogram of body weight after 8-weeks increased more rapidly due to reduced body size rather than increased Wmax capacity (Figure 3). However, the increase in Wmax for each kilogram of body weight after 8-weeks of therapy may not benefit an obese patient's aerobic fitness. Longer pharmacological treatment, which may result in further reductions in body weight, could be effective on increasing aerobic fitness and Wmax production capacity in obese patients.

Physical fitness provides important information on the

risk of death, and small improvements in cardiopulmonary fitness have been shown to be associated with a significantly lowered risk of death even in healthy people (29). Reduced cardiopulmonary fitness, however is associated with an increased mortality rate (30,31). Furthermore, physical activity, which is closely related to physical fitness, has been reported to be inversely associated with blood pressure (32), lipid profiles (33), obesity (34) and insulin sensitivity (35).

It is well known that aerobic fitness levels play an important role in the development of obesity because of their significant association with physical activity. Exercise capacity and aerobic fitness have been shown to be lower in obese patients because of physical inactivity and deconditioning (10). It has also been suggested that aerobic fitness is a marker of later cardiovascular disease with greater aerobic fitness being associated with a reduction in the risk of later cardiovascular disease (36).

In summary, these data indicate that 8-weeks of orlistat and diet therapy have no marked effect on obese patients' Wmax production capacity and aerobic fitness despite more than 5% decrease in body weight and fat mass. Thus, during short-term obesity therapy to improve the impaired aerobic fitness of obese patients, it is important to consider an aerobic exercise training program, which is known to increase aerobic fitness and Wmax capacity, in addition to dieting and pharmacotherapy.

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