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Effects of Short-Term Orlistat Therapy on Maximal Power Production Capacity in Obese Patients

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Abstract: The aim of this study was to examine the effects of weight loss induced by hypocaloric diet and orlistat therapy for a four-week period on maximal work rate (Wmax) production capacity and aerobic fitness in obese patients. Fifteen obese subjects were given an integrated energy restricted diet and orlistat supplement (DO). Each patient performed two incremental ramp exercise tests using an electromagnetically braked cycle ergometer: one at the beginning and one at the end of the four-weeks to determine Wmax production capacity. Four weeks of DO therapy resulted in a significant reduction in total body weight (93.7 ± 14.6 kg vs. 90.3 ± 13.5 kg, P = 0.0001) and body fat mass (37.8 ± 6.4 kg vs. 35.9 ± 7.1 kg, P = 0.003). However, weight reduction achieved during DO therapy was not associated with increased Wmax production capacity: 100 ± 31 W (basal) vs. 103 ± 31 W (four-week) (P = 0.3) and aerobic fitness: 69.2 ± 19 W (basal) vs 66.7 ± 19 W (four-week) (P = 0.5). Body weight reduction without improving obese patients' Wmax production capacity during the DO therapy period indicates that physicians should consider an exercise training program, which is expected to improve obese patients' functional capacity.

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

Introduction

Obesity, defined as body mass index (BMI, weight in kilograms divided by height in m^2) above 30 kg/m^2 due to an increased accumulation of fat mass, is an important risk factor leading to serious medical conditions, including glucose intolerance, increased blood pressure, altered lipid parameters, haemostatic variables and increased insulin resistance (1-3). However, 5-10% weight loss as a result of obesity treatment has been shown to significantly reduce these risk factors (4).

In obesity treatments various pharmacological agents have been introduced as an effective way to reduce body weight. Orlistat (Xenical™) is one of the pharmacological agents promoting weight loss in obese subjects by inhibiting 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).

On the other hand, decreased physical fitness, which is one of the biggest problems in obesity, has been shown to be associated with a marked increase in all causes of mortality (8). It is known that obesity often results in a progressive decline in exercise performance and aerobic fitness because of a vicious cycle of physical inactivity and deconditioning (9). Increased physical fitness thus becomes an important part of obesity treatment in addition to reducing body weight. The effects of short-term orlistat therapy on obese patients' maximal exercise (Wmax) performance and aerobic fitness have not been shown yet.

In the present study, we examined the effects of weight loss induced by four weeks of orlistat therapy combined with a hypocaloric diet (DO) on body composition, Wmax performance and aerobic fitness in obese patients.

Materials and Methods

A total of 15 obese patients (12 female and 3 male), whose body mass index (BMI) varied between 31.4 kg/m^2 and 43.7 kg/m^2 participated. The mean (± SD) values of the patient characteristics are presented in Table 1.

Before the start of the study, all subjects underwent a pre-participation medical exam, including screening for normal glucose tolerance, hormonal analyses (for Cushing's disease and/or hypothyroid etc.), plasma lipid profiles and ECG for cardiovascular risk assessment. They were also screened for any medications known to affect body composition or physical activity. All patients had the risks of the experiment explained to them and signed an informed consent document. The test procedures were approved by the Institutional Review Board for the Use of Human Subjects at the Fırat University Department of Endocrinology and Metabolic Diseases in Elazığ.

Anthropometric measurements were taken of all subjects, including height and weight. During the study, body weight, body mass index (BMI) and body composition were assessed at least once per week between 8 and 10 am using the leg-to-leg bio-electrical impedance method (Tanita Body Fat Analyser, model TBF 300), which has been shown to provide accurate assessments of fat-free mass in obese subjects and changes in fat mass with diet (10).

All obese patients underwent energy restriction with a hypocaloric diet coupled to drug therapy (orlistat 3 x 120 mg/day), which has been reported to be the optimal dosage (11). The energy content of the diet given to the subjects (hypocaloric diet) was 1200-1600 kcal/day (generally, 1400 kcal/day).

The patients fasted overnight (no food or drink) and were also requested to refrain from taking drugs or caffeine for twelve hours 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 two incremental ramp tests as described by Whipp et al. (12) 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 and the second at the end of the four weeks.

The exercise test protocol consisted of three phases: initially, the subjects started pedalling for four minutes at a power of 20 W (60 rpm) as a warm-up period, followed by an incremental period where the work rate was increased by 15 W/min with a work rate controller until the subjects could no longer maintain the work rate, and finally a recovery period where the cycle ergometer power was abruptly reduced back to 20 W and the subjects continued to cycle for another four minutes.

During the exercise test the aerobic to anaerobic metabolic transition point (the anaerobic threshold) was estimated non-invasively using relationships between minute ventilation (V_E l/min, BTPS) to metabolism (13). O_2 consumption (ml/min) in response to the progressively increasing work rate exercise test was estimated indirectly (14). During exercise, V_E, (l, BTPS) and breathing parameters were measured with a spirometer (PONY, COSMED). Throughout the test, the subjects had to wear a heart rate monitor (Polar heart watch) to measure heart beat. Predicted heart rate in obese subjects was estimated using the formula introduced by Miller et al. (15). Heart rate reserve was estimated from the differences between heart rate at maximal exercise performance and at rest.

A paired t test was used to evaluate the statistical significance of differences between values for the basal and four-week levels in both studies. Differences were considered significant at $p < 0.05$.

Results

The changes in body composition four weeks of after progressive supervised therapy with hypocaloric diet and orlistat (DO) are shown in Figure 1.

Four weeks of DO treatment resulted in a significant reduction in total body weight 93.7 ± 14.6 kg (basal) vs. 90.3 ± 13.5 kg (four-week), (i.e. a 3.62% reduction, P

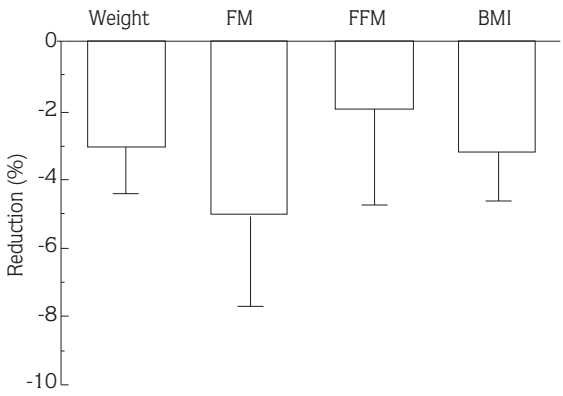

Figure 1. The mean (± SD) reduction of total body weight, fat mass (FM), fat-free mass (FFM) and body mass index (BMI) in response to 4 weeks of diet and orlistat therapy in obese patients. These values reflects the percentage of differences between the basal and four-week periods.

= 0.0001) and BMI 36.1 ± 3.4 kg/m^2 vs. 34.8 ± 3.3 kg/m^2 (i.e. a 3.6% reduction, P = 0.0001), respectively (Table 1). In addition, body fat mass also decreased from 37.8 ± 6.4 kg (basal) to 35.9 ± 7.1 kg (four-week), i.e. a 5.02% reduction (Table 1) (P = 0.003). However, the fat-free mass decrease was not statistically significant: 55.4 ± 11.6 kg (basal) vs. 54.0 ± 10.5 kg (four-week) (Table 1) (P = 0.06).

Table 1. Mean (± SD) values and ranges for patients physical characteristics body weight, body mass index (BMI), fat-free mass (FFM), and fat mass at the onset of the study (basal) and at the end of four weeks of treatment with diet and orlistat.

	Basal (Range)	Four-week (Range)
Age (y)	37.9 ± 9.4 (18-53)	-
Height (cm)	160.8 ± 8.9 (145-183)	-
Weight (kg)	93.7 ± 14.6 (78.5-127.8)	90.3 ± 13.5* (76.8-118)
BMI (kg/m^2)	36.1 ± 3.4 (31.4-43.7)	34.8 ± 3.3* (30.8-42.4)
FFM (kg)	55.4 ± 11.6 (40.9-86)	54.0 ± 10.5 (42.4-82.5)
Fat mass (kg)	37.8 ± 6.4 (29.1-49.2)	35.9 ± 7.1* (28.1-49.7)

* Indicates significant differences from basal values

Reduction in body weight during the four-week therapy period did not have a significant effect on subjects, maximal work rate production capacity (Table 2). The maximal work rate was 100 ± 31 W for the basal and 103 ± 31 W for the four-week test (P = 0.3). Similarly, work rate at the metabolic transition point did not change: 69.2 ± 19 W (basal) vs. 66.7 ± 19 W (four-week) (Table 2) (P = 0.5). In contrast, work production capacity with regard to each kilogram of body weight (Wmax divided by body weight) increased significantly (P = 0.04) from 1.068 ± 0.24 W/kg (basal) to 1.140 ± 0.26 W/kg (four-week) (Table 2, Figure 2). Estimated O_2 uptake did not change significantly: 1773 ± 390 ml/min (basal) vs. 1760 ± 386 ml/min (four-week) (Table 2) (P = 0.5).

Table 2. Mean (± SD) values for maximal work rate production (Wmax), maximal power production capacity with regard to body weight, work rate at the anaerobic threshold (AT) and estimated peak O_2 uptake (VO_2 peak) at the onset of the study (basal) and at the end of the four week treatment period.

	Basal	4 wk
Wmax (W)	100 ± 31	103 ± 31
Wmax/BW (W/kg)	1.068 ± 0.24	1.141 ± 0.26*
AT (W)	69.2 ± 19	66.7 ± 19
VO_2 peak (ml/min)	1773 ± 390	1760 ± 386

* Indicates significant differences from basal values

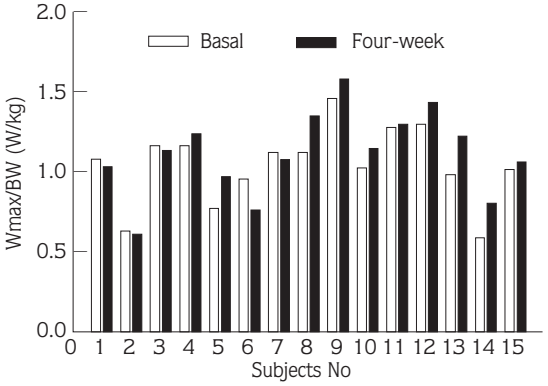

Figure 2. A comparison of obese patients' maximal work production capacities with regard to total body weight at the beginning of the study (white column) and at the end of the four-week period (black column).

The effects of four-week DO therapy on obese patients, heart rate responses to incremental exercise tests are shown in Figure 3. Heart rate at Wmax was 165.2 ± 16 beat/min (basal) (91% of predicted) and 162.5 ± 17 beat/min (four-week) (90% of predicted) (Table 3). Heart rate reserve did not change significantly 79.7 ± 19 beats (basal) and 78.6 ± 17 beats (four-week) (Table 3) (P = 0.3).

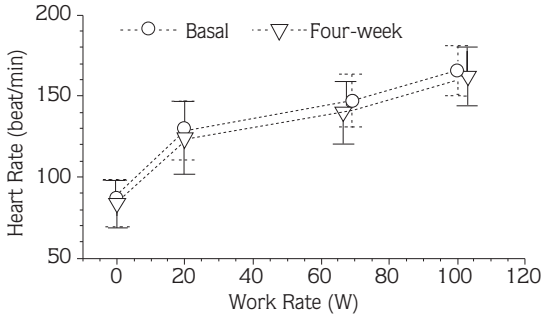

Figure 3. Heart rate response to the progressively increasing work rate exercise test: at rest, during warm-up period, at anaerobic threshold and at maximal exercise performance for the basal (o) and four-week periods (∇).

Discussion

As expected, Wmax production capacity in obese patients was systematically lower than in normal subjects (16,17). Reduced Wmax capacity in obese patients could be related to different factors such as altered muscle fibre type (decreased type I and increased type II) (18),

Table 3. Mean (± SD) values for heart rate at rest, during the warm-up period, at anaerobic threshold, maximal work rate (W_{max}), predicted heart rate and heart rate reserve for the basal and at the end of the four-week periods.

	Rest (beat/min)	Warm-up (beat/min)	AT (beat/min)	Maximal (beat/min)	Predicted (beat/min)	Reserve (beat)
Basal	85.4 ± 13	128.6 ± 18	146.4 ± 17	165.2 ± 16	181.0 ± 4	79.7 ± 19
Four-week	83.8 ± 14	123.9 ± 22	139.9 ± 19	162.5 ± 17	-	78.6 ± 17

cardiovascular factors (reduced left ventricular contractility (19), and pulmonary factors (20).

In our study, despite significantly reduced body weight and fat mass, aerobic fitness as indicated by work rate at the anaerobic threshold and Wmax production capacity did not increase in obese patients. The anaerobic threshold reflecting the aerobic to anaerobic metabolic transition point is a widely used criterion to determine aerobic fitness (21). However, it should be remembered that amount of decrease in total body weight (3.38%) during a short therapy period may be responsible for unaltered aerobic fitness and Wmax production capacity. A longer pharmacological treatment period, which may result in more reduction of body weight, could be effective in increasing aerobic fitness and Wmax production capacity in obese patients. The beneficial effects of modest weight loss (5-10%) on risk factors related to obesity have been shown in previous studies (4, 22).

Physical fitness provides important information on the risk of death, and small improvements in physical fitness have been shown to be associated with a significantly lowered risk of death even in healthy people (23). Furthermore, it has been shown that unfit subjects have a higher risk than fit subjects with similar BMI (24), and that unfit lean men have a higher risk of all-cause mortality than fit but obese ones (25). Fitness thus seems to protect against the influence of these other predictors of mortality (8,25).

Increased physical activity (especially endurance training) is regarded as a fundamentally important component in the prevention and treatment of obesity and its comorbidities (26,27). Furthermore, it has been reported that increased cardiopulmonary fitness in obese patients is an important factor in the mortality rate (28).

We also observed that reduced body weight in response to DO therapy did not have an important effect on the heart rate work rate relationships (Figure 3). The heart rate achieved at Wmax performance was significantly lower than predicted values in both ramp tests. Furthermore, obese patients consumed nearly 50% of their heart rate reserve at a work rate of 20 W cycling, performed as a warm-up period. In obese patients, increased body weight and increased metabolic activity results increased cardiac output, even at rest. Thus, during exercise, increased cardiac output did not correlate with increased metabolic demands (29). It has also been shown that cardiac performance during exercise is an important factor in exercise capacity (30).

In conclusion, reduction in body weight does not of itself increase obese patients, Wmax production capacity and aerobic fitness. An exercise training programme which is known to increase aerobic fitness and work capacity in addition to diet and pharmacological treatment should therefore be added in obesity therapy.

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