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ORIGINAL RESEARCH

Beneficial effects of training at the anaerobic threshold in addition to pharmacotherapy on weight loss, body composition, and exercise performance in women with obesity

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Objective: The aim of this study was to determine and compare the effects of weight loss achieved through orlistat therapy alone or a combination of orlistat and an aerobic exercise training program on aerobic fitness and body composition in obese females.

Methods: Twenty-eight obese patients were randomly assigned to receive 12-week treatment with hypocaloric diet–orlistat or diet–orlistat–exercise. Each participant performed an incremental ramp exercise test every 4 weeks to measure aerobic fitness. Fourteen participants performed continuous exercise (approximately 45 minutes per session) at a work rate corresponding to the anaerobic threshold three times per week.

Results: A decrease in the fat mass to body weight ratio of 3.8% (P=0.006) was observed at the end of the 12 weeks in the orlistat group, while a decrease of 9.5% (P=0.001) was seen in the orlistat–exercise group. Maximal exercise capacity increased by 46.5% in the orlistat–exercise group and by 19.5% in the orlistat group.

Conclusion: While orlistat therapy resulted in an improvement in body composition and aerobic fitness at the end of the 12-week period, its combination with exercise training provided improvements in the same parameters within the first 4 weeks of the study. These additional beneficial effects of combining aerobic exercise with orlistat therapy are important with regards to obesity-associated risk factors.

Keywords: obesity, orlistat, body mass index, anaerobic threshold, aerobic fitness

Introduction

Obesity is a complex, multifactorial disorder characterized by an excess of adipose tissue. It is a serious risk factor for several metabolic disturbances, including type 2 diabetes mellitus, systemic hypertension, dyslipidemia, and coronary artery disease.[1] One of the major problems in obese patients is impaired cardiovascular and metabolic functions, which are closely associated with increased mortality and morbidity.[2,3] The commonly accepted first-line aim in the treatment of obese patients is weight reduction. Even a moderate degree of weight loss, defined as 5%–10% of initial body weight, can reduce obesity-related risk factors.[4]

Orlistat (tetrahydrolipstatin; Xenical™) promotes weight loss by reducing fat uptake from the intestine through gastric and pancreatic lipase inactivation.[5] Pharmacotherapy continues to be investigated as an approach to the treatment of obesity, but this approach has had varying degrees of success. This is because the achievement and maintenance of weight loss within medically accepted optimal ranges is an extremely complex issue.

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Furthermore, it is not clear whether the benefits of moderate weight loss are sustained long term.[6] Importantly, weight loss often causes a reduction in the resting metabolic rate and fat oxidation, which triggers weight regain.[7]

Improvement in aerobic fitness and a change in body composition, rather than weight loss, may have provided important beneficial effects in terms of morbidity and mortality in obesity management. Thus, improvements in cardiopulmonary fitness, in addition to pharmacological obesity treatment, constitute important aspect in the ability to successfully maintain significant long-term weight loss. In addition, physical inactivity may play a pivotal role in impairing the balance between energy intake and energy consumption.[8,9]

The effects of orlistat-induced weight loss on cardiopulmonary fitness, as indicated by an increase in maximal exercise (Wmax) capacity, have not yet been well documented. In the present study, we examined and compared the effects of orlistat therapy with and without aerobic exercise on cardiopulmonary fitness and body composition in obese patients during a 12-week period.

Methods

Participants

Twenty-eight sedentary obese women who sought therapy for obesity at the Obesity Clinic, University of Fırat Hospital, Elazig, Turkey participated in the study. After taking a complete medical history, followed by a physical examination and basic laboratory studies that were conducted at the beginning of the study, only participants who were free of severe medical problems were included. The main exclusion criteria were weight loss of more than 4 kg in the 3 months before screening and a history or presence of significant medical disorders, including diabetes mellitus, cortisone and thyroid abnormality, and cardiovascular diseases. Participants were also screened for taking any medications or circumstances known to affect body composition or physical activity (eg, diuretics, laxatives, antidepressants, acupuncture, and smoking). The study protocol was approved by the Firat University Ethics Committee. After being fully informed of the nature of the experimental protocol, the patients gave their consent to participate and were allowed to enter the study.

General procedures

The patients were maintained on a nutritionally balanced, mildly hypocaloric diet (1,200–1,600 kcal/day). The prescribed diet contained approximately 30% of calories from fat, 50% from carbohydrates, and 20% from protein. The patients received dietary advice from a qualified dietician. During the 12-week study, participants came to the laboratory at least once a week for body weight measurements and dietary advice. The patients were given an orlistat 120 mg capsule to take with each main meal (ie, 3×120 mg/day), which is the recommended therapeutic dose. The patients were randomly categorized into two groups: the orlistat (O) group (number [n]=14; Age: 40.1±2.9 years and height: 156.2±1.7 cm) and the orlistat–exercise (OE) group (n=14; 39.1±2.5 years and 157.5±1.4 cm).

After becoming familiar with the testing equipment, patients performed a symptom-limited maximal exercise test to assess cardiopulmonary and metabolic functional capacity. Each patient performed four incremental ramp tests[10] (one at week 0, one at the end of week 4, one at the end of week 8, and one at the end of week 12) at a work rate of 15 Watt (W)/minute using an electromagnetically braked cycle ergometer (Lode B.V., Groningen, the Netherlands).

The exercise test protocol consisted of three phases. Initially, patients pedaled for 4 minutes at a power of 20 W (60 rpm) as a warm-up period. The work rate was subsequently increased by 15 W/minute with a work rate controller until the patient could no longer maintain the work rate. Finally, patients cycled for a further 4 minutes at 20 W for recovery. The patients' maximal exercise capacity (Wmax) and work rate at the anaerobic threshold were determined for each test. Throughout the test, participants wore 12-lead heart rate monitors to follow electrocardiograms and heartbeat.

Each patient in the OE group performed a constant load exercise (approximately 45 minutes, three times per week). The exercise training intensity was established using the anaerobic threshold, which is the highest point of aerobic energy production without lactic acidosis, and it serves as an important parameter to determine aerobic fitness for patients.[11] The anaerobic threshold was determined using the capillary blood lactate samples (Accutrend® Lactate; Hoffman-La Roche, Basel, Switzerland).

During the 12-week study period, each patient was admitted to the hospital for body composition assessments using the leg-to-leg bioelectrical impedance (Tanita Body Fat Analyzer, TBF 300 M; Tanita, Tokyo, Japan). The measurement of body composition was standardized. All measurements were taken on the same equipment by the same investigator in each assessment. On the mornings of the study visits, the patients were asked about their menstrual status and about their liquid and food intake that morning. The validity and usefulness of bioelectrical impedance in the measurement of body composition in obese patients has been documented.[12]

Statistical analysis

Data are expressed as the mean ± standard error. Comparisons of variables were performed using nonparametric methods because the number of participants in each group was small. The Wilcoxon signed-rank test was used for within-group comparisons of the data, and the Mann–Whitney *U*-test was used to assess between-group data. The statistical differences were considered significant at $P<0.05$.

Results

Body weight, fat mass, and fat-free mass in response to the O and OE groups was not significantly different at the basal level (Table 1). At the end of the 12-week period, the two groups had a marked decrease in body weight of 8.1% (P=0.001) vs 10.6% (P=0.001) and fat mass of 11.9% (P=0.001) vs 19.1% (P=0.001) compared to their baseline levels, respectively. Importantly, the fat mass to body weight ratio showed a marked decrease in the OE group at week 4 (4.4%; P=0.001), at week 8 (8.8%; P=0.001), and at week 12 (9.5%; P=0.001) (Figure 1). However, in the O group, a significant decrease in the fat mass to body weight ratio was observed at the end of week 8 (2.6%; P=0.03) (Figure 1). In the OE group, a significant increase in the fat-free mass to body weight ratio was observed at week 4 (4.0%; P=0.001), at week 8 (7.0%; P=0.001), and at week 12 (8.0%; P=0.001) (Figure 2).

The OE group showed increases in Wmax at week 4 (37.5%; P=0.001), with a continued improvement at week 8 (45.7%; P=0.001) (Table 1). There was no further increase in Wmax capacity at week 12 after its value at week 8 (0.5%) (Table 1). In the O group, Wmax did not increase significantly at week 4, although it did at week 8 (11.2%; P=0.01) and at the end of week 12 (19.5%; P=0.01) (Table 1). The Wmax to body weight ratio was 0.989±0.05 (basal), 1.427±0.05 (week 4; 44.2%; P=0.001), 1.576±0.08 (week 8; 59.3%; P=0.001), and 1.641±0.09 (week 12; 65.9%; P=0.001) in the OE group (Figure 3). In the O group, the Wmax to body weight ratio was 0.970±0.04 at the basal measurement and increased to 1.040±0.05 at week 4 (7.2%; P=0.04). A further significant increase was observed at week 8 (1.133±0.06; 16.8%; P=0.01) and week 12 (1.258±0.05; 29.6%; P=0.001) (Figure 3).

Discussion

The present study was designed to evaluate the efficacy of orlistat therapy combined with aerobic exercise training with respect to body composition and aerobic fitness during a 12-week period. The weight loss obtained from orlistat therapy is an important endpoint in current clinical trials and it is also likely to be associated with considerable health benefits, most notably regarding cardiovascular risk factors. Orlistat therapy had an important effect on the total body weight, even in the first 4 weeks of the study. In the literature, several studies have shown that orlistat vs a placebo induces clinically significant weight loss, as well as improvements in blood lipid parameters and blood pressure in obese individuals.[5,13]

However, note that evaluating the efficacy of weight management strategies depends on identifying outcome goals. Traditionally, such evaluation has focused on total weight loss, but today, more significance has been placed on evaluating improvements in body composition (ie, preserve fat-free mass and lose fat mass) and the improvements in health status (ie, increased aerobic fitness and work capacity).[9,14] A marked improvement in body composition, which represents a decrease in the fat mass to body weight ratio and an increase in the fat-free mass to body weight ratio, may reveal the most effective strategies for addressing the prevention of weight gain in obesity management.[15,16]

There are several reasons for recommending that exercise training be added to an obesity management program.

Table 1 The mean (± SE) values for BMI, body weight, fat mass, FFM, Wmax, work rate at the AT at the beginning of the study (basal), at 4 weeks, at 8 weeks, and at the end of the treatment period with orlistat and orlistat plus exercise

	Orlistat (n=14)				**Orlistat–exercise (n=14)**			
	Basal	**4 weeks**	**8 weeks**	**12 weeks**	**Basal**	**4 weeks**	**8 weeks**	**12 weeks**
BMI (kg/m²)	37.5±0.9	36.2±0.8*	35.5±0.8*	34.5±0.8*	38.6±1.2	37.0±1.3*	35.7±1.2*	34.5±1.2*
Weight (kg)	91.6±2.7	88.3±2.5*	86.6±2.4*	84.1±2.4*	94.7±3.1	90.7±3.3*	87.5±3.2*	84.6±3.3*
Fat mass (kg)	40.3±1.6	38.4±1.6*	37.1±1.4*	35.5±1.5*	42.9±2.4	39.3±2.4*	36.2±2.4*	34.7±2.7*
FFM (kg)	51.6±1.6	49.9±1.0*	49.5±1.1*	49.3±1.4*	51.8±1.0	51.6±1.3^{NS}	51.2±1.1^{NS}	50.0±0.8*
Wmax (W)	87.8±3	90.7±4^{NS}	97.1±4*	105.0±4*	92.1±3	126.7±3*	134.2±4*	135.0±4*
AT (W)	55.0±2	57.8±2*	59.6±3*	68.5±2*	57.8±2	84.2±2*	91.7±2*	92.1±3*

Note: *Significant compared to the basal level.

Abbreviations: SE, standard error; BMI, body mass index; FFM, fat-free mass; Wmax, maximal exercise capacity; AT, anabolic threshold; n, number; NS, not significant compared to basal level; W, watts.

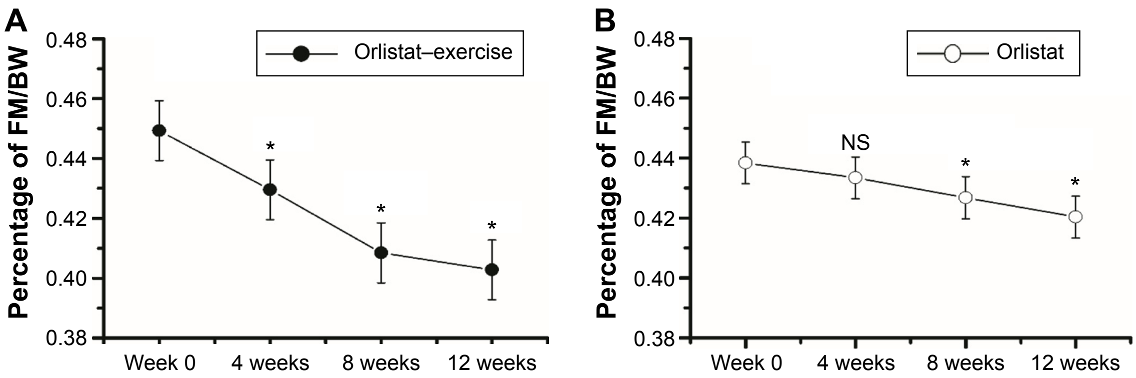

Figure 1 The mean (± SE) values for the patients' FM/BW at the beginning of the study (basal) and after 4 weeks, 8 weeks, and 12 weeks.
Notes: (**A**) Orlistat–exercise group; and (**B**) the orlistat group. *Significant compared to the basal level.
Abbreviations: FM/BW, fat mass to body weight ratio; NS, not significant; SE, standard error.

First, including an aerobic exercise training program with an improved diet and orlistat therapy resulted in a marked decrease in the fat mass to body weight ratio, which can be considered an important criterion to show the effectiveness of a weight loss protocol, even in the first 4 weeks of the study (Figure 1). Furthermore, exercise training also had a significant effect on the fat-free mass to body weight ratio during the study period (Figure 2). The beneficial effects of short-term dieting combined with aerobic exercise training on body composition and physical performance have been documented in obese patients.[17] Aerobic exercise has great potential to speed up the weight loss process by further increasing the amount of energy expended.[15,18] Previous studies have shown that exercise training at the work rate corresponding to the anaerobic threshold results in a marked decrease in fat mass, reflecting an increase in fat oxidation.[17,19]

One key benefit of exercise is the increased calories that are burned beyond resting levels. Furthermore, the resting metabolism does not come back to resting levels immediately after exercise – ie, active individuals may have slightly higher metabolic rates than their sedentary counterparts.[20] Exercise training can also improve sympathetic and parasympathetic nervous activities in the obese patient, which are rather low, and thus help to control obesity.[21] However, dietary-induced weight loss is associated with a decrease in muscle sympathetic nerve activity.[22] In addition to facilitating weight loss, exercise has several other important metabolic effects (eg, improvement of both lipid metabolism and the capacity of the body to handle glucose loads) that are beneficial to obese patients.[23]

Reduced work capacity as a result of low aerobic fitness is a serious consideration in obese patients. Note that an increase in body mass index as a result of increased body fat mass is associated with decreased work production capacity.[24] The low exercise capacity may explain many individuals' short-term success with weight loss, but limited success in long-term

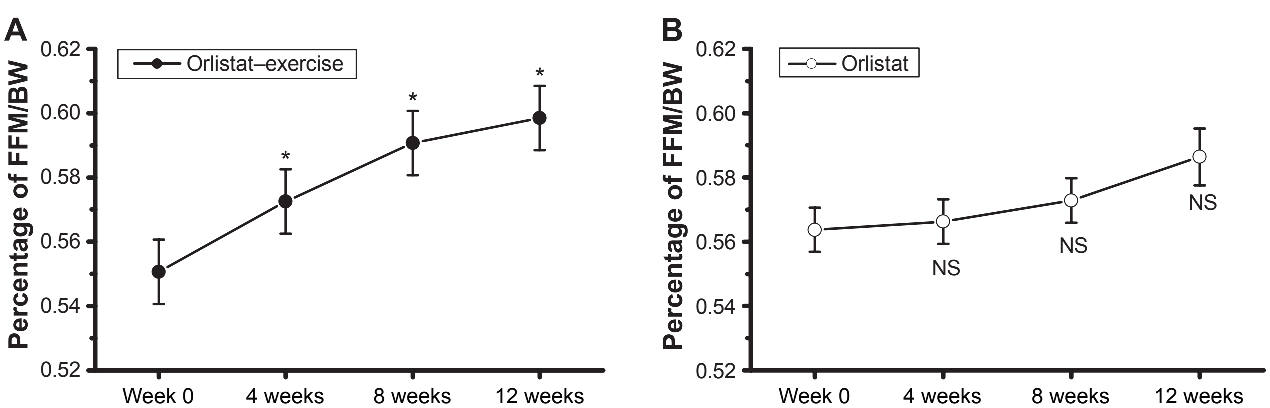

Figure 2 The mean (± SE) values for the patients' FFM/BW at the beginning of the study (week 0) and after 4 weeks, 8 weeks, and 12 weeks for the orlistat–exercise group (black) and the orlistat group (white).
Notes: (**A**) Orlistat–exercise group; (**B**) orlistat group. *Significant compared to the basal level.
Abbreviations: FFM/BW, fat-free mass to body weight ratio; NS, not significant; SE, standard error.

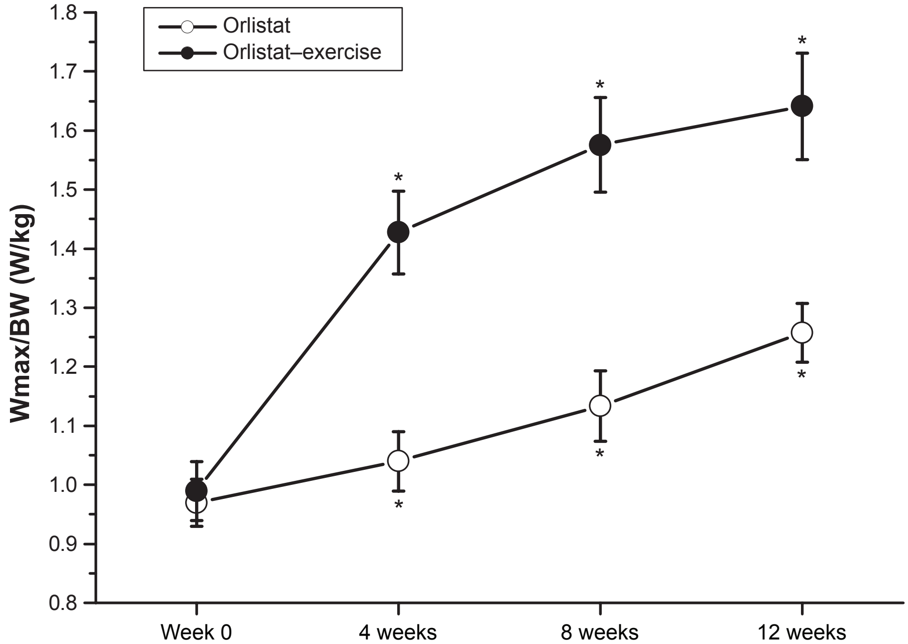

Figure 3 The mean (± SE) values for the patients' Wmax/BW (W/kg) at the beginning of the study (basal) and after 4 weeks, 8 weeks, and 12 weeks for the orlistat group (white) and the orlistat–exercise group (black).
Note: *Significant compared to the basal level.
Abbreviations: Wmax/BW, maximal exercise capacity with regards to total body weight; SE, standard error; W, watts.

weight maintenance. Importantly, weight loss is often associated with a reduction in resting metabolic rate, which is the main risk factor for the later regaining of weight.[8,25]

It is generally accepted that increased physical activity is a cornerstone of obesity management. Aerobic exercise training combined with a low-fat diet can improve the metabolic profile of obese women, despite their adiposity remaining higher than that of lean women.[26] Thus, increased physical activity (especially endurance training) is regarded as a fundamentally important component in the prevention and treatment of obesity and its comorbidities.[27,28] Therefore, with respect to long-term success in weight reduction programs, increased fat mass loss, while preserving fat-free mass (and also resting metabolic rate), is critically important.[29]

The limitation of this study is that the number of patients, who participated is rather low and research with a larger number of patients over a longer time (6–12 months) will provide better results regarding the long-term effects of pharmacotherapy and exercise on weight loss, body composition, aerobic fitness, and also weight regains.

Conclusion

A 12-week orlistat therapy period may provide weight reduction in medically accepted optimal ranges, and it may also improve aerobic fitness in obese patients. The addition of aerobic exercise training with orlistat and an energy-restricted diet program in obese patients has an advantage with respect to changes in body composition (ie, a greater reduction of fat mass and preservation of fat-free mass) and improved aerobic fitness, as indicated by a markedly increased anaerobic threshold and maximal exercise capacity. Aerobic exercise is important for obese patients' health, as well as for losing and maintaining weight and improving aerobic fitness. Considering the large reduction of fat mass and the marked improvement in aerobic fitness, one should consider pharmacotherapy combined with an aerobic exercise training program for sedentary obese patients.

Author contributions

We gratefully declare that all authors participated in the study design, data collection, data analysis, manuscript preparation and revision and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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