Effects of Short-Period Exercise Training and Orlistat Therapy on Body Composition and Maximal Power Production Capacity in Obese Patients

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Summary

We examined the effects of weight loss induced by diet-orlistat (DO) and diet-orlistat combined with exercise (DOE) on maximal work rate production (W_max) capacity in obese patients. Total of 24 obese patients were involved in this study. Twelve of them were subjected to DO therapy only and the remaining 12 patients participated in a regular aerobic exercise-training program in addition to DO therapy (DOE). Each patient performed two incremental ramp exercise tests up to exhaustion using an electromagnetically-braked cycle ergometer: one at the onset and one at the end of the 4th week. DOE therapy caused a significant decrease in total body weight: 101.5 ± 17.4 kg (basal) vs 96.3 ± 17.3 kg (4 wk) associated with a significant decrease in body fat mass: 45.0 ± 10.5 kg (basal) vs 40.9 ± 9.8 kg (4 wk). DO therapy also resulted in a significant decrease of total body weight 94.9 ± 14.9 kg (basal) vs 91.6 ± 13.5 kg (4 wk) associated with small but significant decreases in body fat mass: 37.7 ± 5.6 kg (basal) to 36.0 ± 6.2 kg (4 wk). Weight reduction achieved during DO therapy was not associated with increased W_max capacity: 106 ± 32 W (basal) vs 106 ± 33 W (4 wk), while DOE therapy resulted in a markedly increased W_max capacity: 109 ± 39 W (basal) vs 138 ± 30 W (4 wk). DO therapy combined with aerobic exercise training resulted in a significant reduction of fat mass tissue and markedly improved the aerobic fitness and W_max capacities of obese patients. Considering this improvement within such a short period, physicians should consider applying an aerobic exercise-training program to sedentary obese patients for improving their physical fitness and thereby reduce the negative outcomes of obesity.

Key words

Obesity • Body mass index • Aerobic exercise intensity

Introduction

Obesity is a chronic disease, which results from a disrupted balance between energy intake and energy consumption, the excess energy being stored in the adipose tissues (Flatt et al. 1985, Doucet and Tremblay 1997). The effective treatment of obesity still remains to be one of the greatest challenges in clinical medicine. This is because obesity is an important risk factor leading to serious medical problems associated with increased mortality (Pi-Sunyer 1993, Chan et al. 1994, Kannel et al. 1996, Jung 1997). In obesity treatment, caloric restriction and increased physical activity are generally recommended...
weight-reduction programs, which alter energy intake to energy consumption ratio. In addition to the diet and physical activity, pharmacological agents have also been introduced as an effective way for treatment of obesity. Orlistat (Xenical™) is a pharmacological agent promoting weight loss in obese patients by inhibiting pancreatic lipase (Uusitupa 1999). The specific effects of orlistat therapy on body weight and body composition have been shown in previous long-term studies (James et al. 1997, van Gaal et al. 1998, Davidson et al. 1999). One of the largest problems in obese patients is a progressive reduction in their fitness as a result of increased body mass index (BMI) associated with increased fat mass and decreased physical activity. In addition, increased BMI is more likely to lead to serious limitations in performing basic daily activities. It is known that there is an inverse relationship between obese patients’ aerobic capacity and the fat mass ratio (Lee et al. 1999). Furthermore, low level of physical activity and decreased physical fitness have been shown to be associated with a marked increase in all causes of mortality rates (Blair et al. 1995). Thus, it is logical to consider the improvement of physical fitness rather than the reduction of body weight alone when treating obese patients.

In the present study, we examined the effects of weight loss induced by DO therapy or DOE therapy during a 4-week period on W_max capacity and aerobic fitness in obese patients.

Table 1. Physical characteristics of the subjects, body weight, body mass index (BMI), fat free mass (FFM), fat mass at the onset of the study (basal) and at the end of 4-week treatment period with diet and orlistat (DO) and diet, orlistat plus exercise (DOE).

<table>
<thead>
<tr>
<th></th>
<th>Diet + Orlistat (n=12)</th>
<th>Diet + Orlistat + Exercise (n=12)</th>
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<tbody>
<tr>
<td></td>
<td>Basal 4 wk P</td>
<td>Basal 4 wk P</td>
</tr>
<tr>
<td>Age (years)</td>
<td>38.3±10 (18-53)</td>
<td>37.5±8 (19-47)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.9±9 (145-183)</td>
<td>159.7±10 (150-189)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>94.9±14.9 (78.5-127.8)</td>
<td>91.6±13.5 (76.8-118)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>36.1±3.6 (31.4-43.7)</td>
<td>34.9±3.4 (30.8-42.4)</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>56.7±12.6 (40.9-86)</td>
<td>55.1±11.5 (42.4-82.5)</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>37.7±5.6 (29.1-49.2)</td>
<td>36.0±6.2 (28.1-49.7)</td>
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The data are means ± S.D., values in parentheses represent ranges.

Methods

The protocol of this study was approved by the local Ethics Committee and informed consent was obtained from all participating patients. Total of 24 obese patients (21 females and 3 males) were involved in this study. Demographic characteristics of patients are presented in Table 1. All patients underwent an initial medical examination, including screening for normal glucose tolerance, hormonal analyses (e.g. cortisone, thyroid), plasma lipid profile and ECG for cardiovascular risk assessment. They were also screened for taking any medications known to affect body composition or physical activity. The excluding criteria were as follows: abnormal glucose tolerance, cortisone, thyroid and ECG abnormalities.

During a 4-week period, the body weight, body mass index (BMI) and body composition were assessed using the leg-to-leg bioelectrical impedance method (Tanita Body Fat Analyser, model TBF 300) which has been shown to provide accurate assessment of fat free mass in obese patients and changes in fat mass with the diet or combined with exercise (Utter et al. 1999).

The patients were also requested to refrain from taking any drugs or caffeine for a period of 12 h before the test. After becoming familiar with the testing equipment, a trial limited maximal exercise test was performed by each patient to assess cardiopulmonary and
between minute ventilation ($V_E$, l/min) and metabolism was estimated non-invasively using the close relationship metabolic transition point (or the anaerobic threshold) body weight was also measured. Aerobic to anaerobic work rate production capacity with regard to the total capacity relative to the total body weight. The aerobic The patients’ fitness was measured using $W_{max}$ the patient continued to cycle for further four minutes. Lastly, a recovery period in which the cycle ergometer power was reduced abruptly again to 20 W and the patient continued to cycle for further four minutes. The patients’ fitness was measured using $W_{max}$ capacity relative to the total body weight. The aerobic work rate production capacity with regard to the total body weight was also measured. Aerobic to anaerobic metabolic transition point (or the anaerobic threshold) was estimated non-invasively using the close relationship between minute ventilation ($V_E$, l/min) and metabolism (Wasserman et al. 1973, Hollmann 1985). During the incremental exercise test, $V_E$ increases in proportion to the increase in metabolic demands of the exercising muscles. At the onset of metabolic (mainly lactic) acidosis which results from anaerobic metabolism, $V_E$ increases out of proportion to the work rate (Wasserman et al. 1994).

In this study, patients were randomly divided into two groups as follows:

DO: Twelve subjects had energy restriction on a mild hypocaloric diet coupled to orlistat therapy. The obese patients received orlistat 120 mg three times a day, which is the most effective dosage (van Gaal et al. 1998). The energy content of the diet of the obese patients (mild hypocaloric diet) was 1200-1600 kcal/day. During the study period, the control of the patients diet was based on personal communication.

DOE: In addition to DO therapy, 12 patients enrolled to this group performed an intensive regular exercise training. The training work rate was set to the anaerobic threshold and performed three times per week, over 4 weeks. Each training session lasted 35-45 min. However, we used 50-70 % of $W_{max}$ to establish the training work rate, since the non-invasive technique used in this study does not correspond exactly to the anaerobic threshold estimation.

$O_2$ consumption (ml/min) in response to the progressively increasing work rate exercise test was estimated indirectly (Wasserman and Whipp 1975). During exercise, $V_E$ (l/min, at body temperature saturated with water vapor at ambient pressure, BTPS) and breathing parameters were measured with a spirometer (Pony, Cosmed). The heart rate was monitored throughout the test using a Polar heart watch (Polar Favor).

The data are expressed as means ± S.D. Paired t test was used to evaluate the statistical significance of differences between the mean basal values and after 4 weeks in both groups. Differences were considered significant at p<0.05.

### Results

The changes in body composition after 4 weeks of progressive supervised therapy with DO and DOE are shown in Table 1. The changes in BMI during 4-week period were 36.1±3.6 kg/m² vs. 34.9±3.4 kg/m² (3.41 % reduction) for the DO group (P=0.0001) and 39.8±5.4 kg/m² vs. 37.7±5.5 kg/m² (5.23 % reduction) for the DOE group (P=0.0001) (Table 1). DOE treatment resulted in a significant decrease in total body weight (P=0.0001): 101.5±17.4 kg (basal) vs. 96.3±17.3 kg (4 wk), (5.12 % reduction) (Fig. 1). This reduction in total body weight was associated with significant decreases (4.1 kg, 9.11 %) in body fat mass (P=0.0001): 45.0±10.5 kg (basal) vs. 40.9±9.8 kg (4 wk) (Table 1). The systematic reduction in body fat mass was observed in all DOE-treated patients (Fig. 2). There was no significant change in fat free mass (P=0.2) during 4 weeks of therapy: 56.5±10.5 kg (basal) vs. 55.5±10.3 kg (4 wk) (Table 1).

The 4-week DO treatment also resulted in a significant reduction in total body weight (P=0.001): 94.9±14.9 kg (basal) vs. 91.6±13.5 kg (4 wk), (i.e. 3.47 % reduction) (Table 1). In addition, body fat mass was also reduced significantly (P=0.02) from 37.7±5.6 kg (basal) to 36.0±6.2 kg (4 wk), i.e. 4.50 % reduction (Table 1). However, the percentage reduction in body fat mass differed among the subjects (Fig. 1). There was an increase in body fat mass ratio in two subjects and no change in one subject, while another subject had 15 % reduction (Fig. 1). Fat free mass decreased, but this decrease was not significant: 56.7±12.6 kg (basal) vs. 55.1±11.5 kg (4 wk) (Table 1).

In the DOE group, there was a systematic increase in the maximal work rate in all subjects (Fig. 3). The subjects’ $W_{max}$ production capacity (expressed in watts) increased significantly (P=0.0001) by 26.6 % after 4 weeks training period: from 109±39 W (basal) to
138±30 W (4 wk) (Table 2). In addition, the work rate production capacity (expressed per kilogram body weight) increased significantly (P=0.0001) in DOE group by approximately 35 %: from 1.086±0.31 W/kg (basal) to 1.465±0.28 W/kg (4 wk) (Table 2). The work rate at the metabolic transition point (anaerobic threshold) increased by about 25 % in DOE group (P=0.001): 67±19 W (basal) vs. 84±16 W (4 wk) (Table 2). In the present study, it was not possible to estimate the anaerobic threshold in two subjects at basal and one subject at 4 weeks in the DO group and two subjects at the basal period in the DOE group.

Reduction of body weight by DO therapy did not have a significant effect on subjects W_max capacity (Fig. 2) and W_max capacity per kilogram body weight (Fig. 3). W_max and its relationship to body weight were found to be 106±32 W and 1.114±0.22 W/kg for the basal and 106±33 W and 1.162±0.27 W/kg for the end of 4-week period, respectively (Table 2). Similarly, work rate at the metabolic transition point did not change significantly: 72±30 W (basal) vs. 70±19 W (4 wk) (Table 2).
Estimated $O_2$ uptake did not change significantly in DO group: $1773 \pm 390$ ml/min (basal) vs. $1760\pm386$ ml/min (4 wk) (Table 2). However, $O_2$ uptake increased significantly (P=0.0001) from $1842\pm440$ ml/min (basal) to $2109\pm357$ ml/min (4 wk) in the DOE group (Table 2).

**Table 2.** Maximal work rate production ($W_{max}$), maximal power production capacity with regard to body weight ($W_{max}/BW$), work rate at the anaerobic threshold (AT) and estimated peak $O_2$ uptake ($V_{O2}$peak) at the onset of the study (basal) and at the end of the 4-week treatment period with diet and orlistat and diet, orlistat plus exercise.

<table>
<thead>
<tr>
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<th>Diet + Orlistat + Exercise (n=12)</th>
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<tbody>
<tr>
<td></td>
<td>Basal</td>
<td>4 wk</td>
</tr>
<tr>
<td>$W_{max}$ (W)</td>
<td>106±32</td>
<td>106±33</td>
</tr>
<tr>
<td>$W_{max}/BW$ (W/kg)</td>
<td>1.11±0.22</td>
<td>1.16±0.27</td>
</tr>
<tr>
<td>AT (W)</td>
<td>72±30</td>
<td>70±19</td>
</tr>
<tr>
<td>$V_{O2}$peak (ml/min)</td>
<td>1773±390</td>
<td>1760±386</td>
</tr>
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</table>

Data are means ± S.D.

### Discussion

The results of this study showed that a combination of an aerobic exercise training program with drug and diet therapy resulted in a marked reduction of total body weight and body fat mass during a 4-week period. These findings are consistent with the result of previous studies where a negative energy balance induced by exercise resulted in an increased loss of fat mass compared to negative energy balance induced by a diet and/or drug in obese patients (Sopko et al. 1985, Ross et al. 2000). A decreased fat mass during aerobic exercise training program has been reported as a result of increased fat oxidation (Martin et al. 1994, Phillips et al. 1996). Interestingly, increased fat oxidation has been reported as early as after five days of aerobic training program (Phillips et al. 1996). It is well known that exercise training stimulates the mobilization and oxidation of fatty acids (Romjin et al. 1993). Thus, a combination of moderate intensity exercise training program with obesity therapy enhances fat oxidation (van Baak 1999), and may also influence blood lipid profiles (Berg et al. 1994).

It has been shown that long-term treatment is required to establish the therapeutic effects of orlistat in obesity treatment (van Gaal et al. 1998, Davidson et al. 1999). We have found an approximately 3.5 % decrease in total body weight with 4 weeks of orlistat treatment which is comparable with report of van Gaal et al. (1998). However, total body weight loss and fat mass reduction varied widely among the patients who received DO therapy (Fig. 1). This result highlights the variation in individual patients responses to pharmacological therapy of obesity which was not observed in the aerobic exercise training group (Fig. 1).

It is known that obesity often results in a progressive decline in exercise capacity and aerobic fitness, because of the vicious cycle of physical inactivity and deconditioning (Bouchard and Shephard 1994, Jebb and Moore 1999). Thus, increased physical activity (especially endurance training) is regarded as a fundamentally important component in the prevention and treatment of obesity and its comorbidities (Barlow et al. 1995, DiPietro 1999, Grundy et al. 1999). Furthermore, it has been shown that physical inactivity is an important factor that contributes to obesity at all stages in life (Shephard 1995).

Our results confirmed that the combination of an energy restricted diet, orlistat and an aerobic exercise training program (at a work rate corresponding to the anaerobic threshold) appears to significantly improve both $W_{max}$ capacity and aerobic capacity. These were shown by a marked increase in the work rate to exhaustion (by 26 %) and work rate to anaerobic threshold (by 25 %) in obese patients during a 4 weeks period.

The short-term positive effect of a combination of the diet and exercise therapy on both aerobic capacity and $W_{max}$ capacity in obese patients is in agreement with the results of Sartorio et al. (2001). Importantly, fat-free
mass was not enhanced significantly while fat mass loss was enhanced by exercise training which is the primary objective of various obesity treatment protocols (Evans et al. 1999).

It has been reported that aerobic exercise training with or without a diet can improve aerobic fitness without significantly affecting body composition in obese patients (Utter et al. 1998). The marked improvement of maximal work rate production capacity in obese patients during a 4-week period of DOE therapy is probably due to the performed aerobic exercise rather than to weight loss. Therefore, weight loss achieved during 4-week period (as 3.5%) does not seem to be absolutely necessary for improvement in \( W_{\text{max}} \) capacity in obese patients.

However, it should be mentioned that amount of total body weight reduction, which requires a rather long therapy period with DO, may be important for increasing physical fitness in obese patients. In previous studies, obesity-associated risk factors have been reported to be reduced even after a modest (5-10%) body weight loss (Goldstein 1992, Pi-Sunyer 1996, van Gaal et al. 1997).

It has been widely demonstrated that an aerobic exercise training can increase the aerobic capacity and also maximal work production capacity in subjects with different fitness conditions including normal sedentary (Davis et al. 1979), elderly people (Belman and Gaesser 1991), patients with heart diseases (Coyle et al. 1983) or lung diseases (Casaburi et al. 1995).

In our study, patients’ exercise intensity was established using anaerobic threshold, which is the optimal work rate for training and is an important parameter for determination of the fitness level in individual patients (Hansen et al. 1984, Wasserman et al. 1994). Estimation of the anaerobic threshold during exercise performance is an important criterion as it can be used as an index of aerobic fitness in both patients (Older et al. 1993, Patessio et al. 1993) and normal healthy subjects (Davis et al. 1979). The anaerobic threshold reflects the highest point for body energy production provided by aerobic metabolism, i.e. for determining the highest oxidative phosphorylation capacity without a glycolytic energy supply (Wasserman et al. 1994).

In previous studies, it has been reported that unfit subjects are at a higher risk compared to fit subjects with a similar BMI (Lee et al. 1998) and that also unfit lean men are at a higher risk of all-cause of mortality than fit obese subjects (Lee et al. 1995). Thus, fitness of the subject seems to protect against the influence of other predictors of mortality (Blair et al 1995, Lee et al. 1995).

As a result, the performance of a short-term aerobic exercise training program in combination with DO therapy leads to two important changes: 1) a proportionally greater reduction in body fat mass, and 2) improving patients aerobic fitness and maximal work production capacities. Considering this improvement in \( W_{\text{max}} \) capacity and work rate at the anaerobic threshold in such a short-term therapy period, physicians should consider an aerobic exercise training program to sedentary obese patients to become physically active and thereby to reduce the negative effects of obesity.

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References


Reprint requests
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