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

R. COLAK[1], O. OZCELIK[2]

[1]Department of Endocrinology and Metabolism, [2]Department of Physiology, Firat University Faculty of Medicine, Elazig, Turkey

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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

Fax +420 241 062 164
E-mail: physres@biomed.cas.cz http://www.biomed.cas.cz/physiolres

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^{TM}) 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).

	Diet + Orlistat (n=12)			Diet + Orlistat + Exercise (n=12)		
	Basal	**4 wk**	**P**	**Basal**	**4 wk**	**P**
Age (years)	38.3±10 (18-53)	–		37.5±8 (19-47)	–	
Height (cm)	161.9±9 (145-183)	–		159.7±10 (150-189)	–	
Weight (kg)	94.9±14.9 (78.5-127.8)	91.6±13.5 (76.8-118)	0.001	101.6±17.4 (82.2-138)	96.3±17.3 (74.6-129.5)	0.0001
BMI (kg/m^2)	36.1±3.6 (31.4-43.7)	34.9±3.4 (30.8-42.4)	0.0001	39.8±5.4 (30.6-50.6)	37.7±5.5 (27.7-47.9)	0.0001
FFM (kg)	56.7±12.6 (40.9-86)	55.1±11.5 (42.4-82.5)	0.1	56.5±10.5 (47.4-88.3)	55.5±10.3 (46.1-84.3)	0.2
Fat mass (kg)	37.7±5.6 (29.1-49.2)	36.0±6.2 (28.1-49.7)	0.02	45.0±10.5 (29-67)	40.9±9.8 (25.4-60.2)	0.0001

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

metabolic functional capacity. Each patient performed two incremental ramp tests (Whipp *et al.* 1981) at a work rate 15 W/min using an electromagnetically braked cycle ergometer (LODE, Groningen, The Netherlands): one at the onset of study and the other at the end of the 4th week.

The exercise test protocol consisted of three phases. Initially, patients started to pedal for 4 min at a power of 20 W (60 rpm) as a warm-up period. Then, an incremental period during which the work rate was increased by 15 W/min with a work rate controller until the patients could no longer continue to maintain the work rate. 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 Wmax 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/m^2 vs. 34.9±3.4 kg/m^2 (3.41 % reduction) for the DO group (P=0.0001) and 39.8±5.4 kg/m^2 vs. 37.7±5.5 kg/m^2 (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.

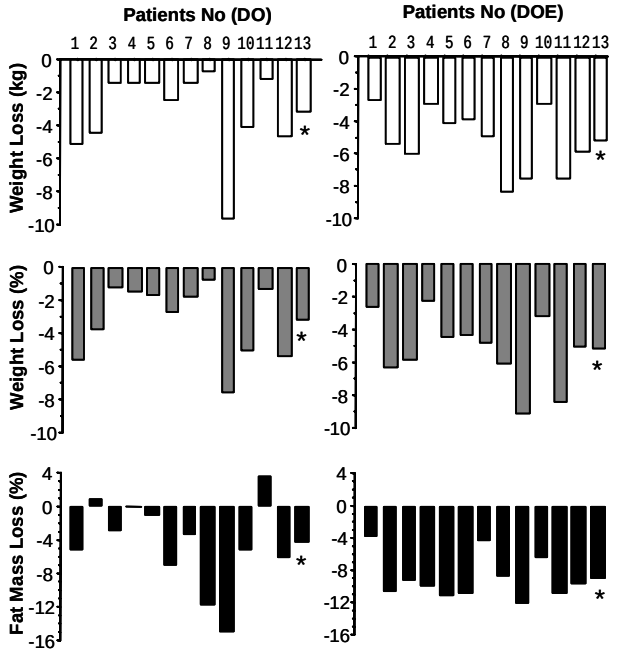

Fig. 1. The effects of 4 weeks diet and orlistat therapy (DO) and diet, orlistat plus exercise therapy (DOE) on patients' total body weight loss (white), percentage of weight loss (gray) and percentage of fat mass loss (black). These values reflect the differences between basal and 4-week therapy period; * mean values.

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).

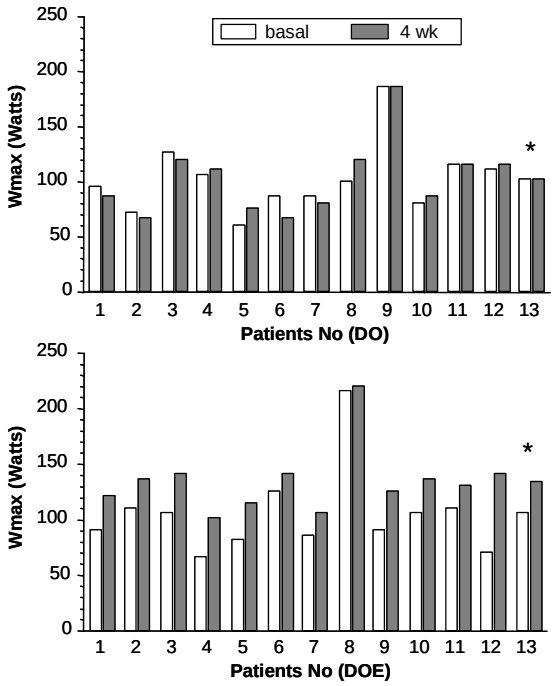

Fig. 2. The subjects' maximal work rate production capacities at the onset of study (white) and at the end of the 4-week period (gray) in response to the therapy with diet and orlistat (DO) and diet, orlistat plus exercise (DOE), * mean values.

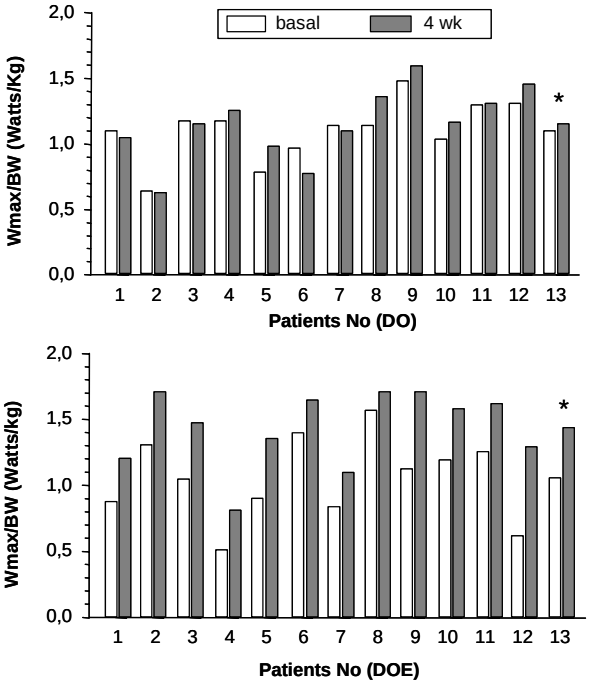

Fig. 3. The comparison of the patients maximal work rate production capacities with regard to the total body weight at the onset of study (white) and at the end of the 4-week period (gray) for diet and orlistat (DO) and for diet, orlistat plus exercise (DOE), * mean values.

Estimated O_2 uptake did not change significantly in DO group: 1773 ± 390 ml/min (basal) vs. 1760±386 ml/min (4 wk) (Table 2). However, O_2 uptake increased significantly (P=0.0001) from 1842±440 ml/min (basal) to 2109±357 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 (VO_2 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.

	Diet + Orlistat (n=12)			Diet + Orlistat + Exercise (n=12)		
	Basal	**4 wk**	**P**	**Basal**	**4 wk**	**P**
W_{max} (W)	106±32	106±33	0.8	109±39	138±30	0.0001
W_{max}/BW (W/kg)	1.114±0.22	1.162±0.27	0.2	1.086±0.31	1.465±0.28	0.0001
AT(W)	72±30	70±19	0.7	67±19	84±16	0.001
VO_2 peak (ml/min)	1773±390	1760±386	0.8	1842±440	2109±357	0.0001

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 be 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_{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_{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

BARLOW CE, KOHL HW, GIBBONS LW, BLAIR SN: Physical fitness, mortality and obesity. *Int J Obes Relat Metab Disord* **19** (Suppl 4): S41-S44, 1995.

BELMAN MJ, GAESSER GA: Exercise training below and above the lactate threshold in elderly. *Med Sci Sports Exerc* **23**: 562-568, 1991.

BERG A, FREY I, BAUMSTARK M, HALLE M, KEUL J: Physical activity and lipoprotein disorders. *Sports Med* **17**: 6-21, 1994.

BLAIR SN, KOHL III HW, BARLOW CE, PAFFENBARGER RS JR, GIBBONS LW, MACERA CA: Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *JAMA* **273**:1093-1098, 1995.

BOUCHARD C, SHEPHARD RJ: Physical activity, fitness and health: the model and key concepts. In: *Physical Activity, Fitness, and Health: International Proceedings and Consensus Statement*. BOUCHARD C, SHEPHARD RJ , STEPHENS T (eds), Human Kinetics, Champaign, IL, 1994, pp 77-88.

CASABURI R, STORER TW, SULLIVAN CS, WASSERMAN K: Evaluation of blood lactate elevation as an intensity criterion for exercise training. *Med Sci Sports Exerc* **27**: 852-862, 1995.

CHAN JM, RIMM EB, COLDITZ GA, STAMPFER MJ, WILLETT WC: Obesity, fat distribution, and weight gain as a risk factors for clinical diabetes in man. *Diabetes Care* **17**: 961-969, 1994.

COYLE EF, MARTIN WH, EHSANI AA, HAGBERG JM, BLOOMFIELD SA, SINACORE DR, HOLLOSZY JM: Blood lactate threshold in some well-trained ischemic heart disease patients. *J Appl Physiol* **54**: 18-23, 1983.

DAVIDSON MH, HAUPTMAN J, DIGRILAMO M, FOREYT JP, HALSTED CH, HEBER D, HEIMBURGER DC, LUCAS CP, ROBBINS DC, CHUNG J, HEYMSFIELD SB: Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat. *JAMA* **281**: 235-242, 1999.

DAVIS JA, FRANK MH, WHIPP BJ, WASSERMAN K: Anaerobic threshold alterations caused by endurance training in middle-aged men. *J Appl Physiol* **46**: 1039-1046, 1979.

DIPIETRO L: Physical activity in the prevention of obesity: current evidence and research issues. *Med Sci Sports Exerc* **31** (Suppl 11): S542-S546, 1999.

DOUCET E, TREMBLAY A: Food intake, energy balance and body weight control. *Eur J Clin Nutr* **51**: 846-855, 1997.

EVANS EM, SAUNDERS MJ, SPANO MA, ARNGRIMSSON SA, LEWIS RD, CURETON KJ: Effects of diet and exercise on the density and composition of fat-free mass in obese women. *Med Sci Sports Exerc* **31**: 1778-1787, 1999.

FLATT JP, RAVUSSIN E, ACHESON KJ, JEQUIER E: Effects of dietary fat on postprandial substrate oxidation and on carbohydrate and fat balance. *J Clin Invest* **76**: 1019-1024, 1985.

GOLDSTEIN DJ: Beneficial health effects of modest weight loss. *Int J Obes Relat Metab Disord* **16**: 397-415, 1992.

GRUNDY SM, BLACKBURN G, HIGGINS M, LAUER R, PERRI MG, RYAN D: Physical activity in the prevention and treatment of obesity and its comorbidities: evidence report of independent panel to assess the role of physical activity in the treatment of obesity and its comorbidities. *Med Sci Sports Exerc* **31**: 1493-1500, 1999.

HANSEN JE, SUE DY, WASSERMAN K: Predicted values for clinical exercise testing. *Am Rev Respir Dis*; **129** (suppl): S49-55, 1984.

HOLLMANN W: Historical remarks on the development of the anaerobic threshold up to 1966. *Int J Sports Med* **6**: 109-116, 1985.

JAMES WP, AVENELL A, BROOM J, WHITEHEAD J: A one-year trial to assess the value of orlistat in the management of obesity. *Int J Obes Relat Metab Disord* **21** (Suppl 3): S24-S30, 1997.

JEBB SA, MOORE MS: Contribution of a sedentary lifestyle and inactivity to the etiology of overweight and obesity: current evidence and research issues. *Med Sci Sports Exerc* **31** (Suppl 11): S534-S541, 1999.

JUNG RT: Obesity as a disease. *Br Med Bull* **53**: 307-321, 1997.

KANNEL WB, D'AGOSTINO RB, COBB JL: Effects of weight on cardiovascular disease. *Am J Clin Nutr* **63** (Suppl): 419S-422S, 1996.

LEE IM, HSIEH CC, PAFFENBARGER RS JR: Exercise intensity and longevity in men. The Harvard Alumni Health Study. *JAMA* **273**: 1179-1184, 1995.

LEE CD, JACKSON AS, BLAIR SN: US weight guidelines: is it also important to consider cardiorespiratory fitness? *Int J Obes Relat Metab Disord* **22** (Suppl 2): S2-S7, 1998.

LEE CD, BLAIR SN, JACKSON AS: Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr* **69**: 373-380, 1999.

MARTIN WH, DALSKY GP, HURLEY BF, MATHEWS DE, BIER DM, HAGBERG JM, ROGERS MA, KING DS, HOLLOSZY JO: Effects of endurance training on free fatty acid turnover and oxidation during exercise. *Am J Physiol* **265**: E708-E714, 1994.

OLDER P, SMITH R, COURTNEY P, HONE R.: Preoperative evaluation of cardiac failure and ischemia in elderly patients by cardiopulmonary exercise testing. *Chest* **104**: 701-704, 1993.

PATESSIO A, CASABURI R, CARONE M, APPENDINI L, DONNER CF, WASSERMAN K: Comparison of gas exchange, lactate and lactic acidosis thresholds in patients with chronic obstructive pulmonary disease. *Am Rev Respir Dis* **148**: 622-626, 1993.

PHILLIPS SM, GREEN HJ, TARNOPOLSKY MA, HEIGENHAUSER GJF, HILL RE, GRANT SM: Effects of training duration on substrate turnover and oxidation during exercise. *J Appl Physiol* **81:** 2182-2191, 1996.

PI-SUNYER FX: Medical hazards of obesity. *Ann Intern Med* **119**: 655-660, 1993.

PI-SUNYER XA: A review of long-term studies evaluating the efficacy of weight loss in ameliorating disorders associated with obesity. *Clin Ther* **18**: 1006-1036, 1996.

ROMJIN JA, COYLE EF, SIDOSSIS L, GASTALDELLI A, HOROWITZ JF, ENDERT E, WOLFE RR: Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity. *Am J Physiol* **265**: E380-E391, 1993.

ROSS R, DAGNONE D, JONES PJH, SMITH H, PADDAGS A, HUDSON R, JANSSEN I: Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men: a randomised controlled trial. *Ann Intern Med* **133**: 92-103, 2000.

SARTORIO A, NARICI MV, FUMAGALLI E, FAGLIA G, LAFORTUNA CL: Aerobic and anaerobic performance before and after a short-term body mass reduction program in obese subjects. *Diabetes Nutr Metab* **14**:51-57, 2001.

SHEPHARD RJ: Physical activity, health and well-being at different life stages. *Res Q Exerc Sport* **66**: 298-302, 1995.

SOPKO G, LEON AS, JACOBS DR, FOSTER N, MOY J, KUBA K, ANDERSON JT, CASAL D, MCNALLY C, FRANTZ I: The effects of exercise and weight loss on plasma lipids in young obese men. *Metabolism* **34**: 227-236, 1985.

UTTER AC, NIEMAN DC, SHANNONHOUSE EM, BUTTERWORTH DE, NIEMAN CN: Influence of diet and/or exercise on body composition and cardiorespiratory fitness in obese women. *Int J Sport Nutr* **8**: 213-222, 1998.

UTTER, AC, NIEMAN DC, WARD AN, BUTTERWORTH DE: Use of the leg-to-leg bioelectrical impedance method in assessing body composition change in obese women. *Am J Clin Nutr* **69**: 603-607, 1999.

UUSITUPA M: New aspects in management of obesity: operation and impact of lipase inhibitors. *Curr Opin Lipidol* **10**: 3-7, 1999.

VAN BAAK MA: Exercise training and substrate utilisation in obesity. *Int J Obes Relat Metab Disord* **23** (Suppl 3): S11-S17, 1999.

VAN GAAL LF, BROOM JI, ENZI G, TOPLAK H. Efficacy and tolerability of orlistat in the treatment of obesity: a 6 month dose-ranging study. *Eur J Clin Pharmacol* **54**: 125-132, 1998.

VAN GAAL LF, WAUTERS MA, DE LEEUW ICH: The beneficial effects of modest weight loss on cardiovascular risk factors. *Int J Obes Relat Metab Disord* **21** (Suppl 1): S5-S9, 1997.

WASSERMAN K, WHIPP BJ: Exercise physiology in health and disease. *Am Rev Respir Dis* 112: 219-249, 1975.

WASSERMAN K, WHIPP BJ, KOYAL SN, BEAVER WL: Anaerobic threshold and respiratory gas exchange during exercise. *J Appl Physiol* **35**:236-243, 1973.

WASSERMAN K, HANSEN JE, SUE DY, WHIPP BJ: *Principles of Exercise Testing and Interpretation.* JM HARRIS (ed), Lea & Febiger, Philadelphia, 1994, pp 52-72.

WHIPP BJ, DAVIS JA, TORRES F, WASSERMAN K: A test to determine parameters of aerobic function during exercise. *J Appl Physiol* **50**: 217-221, 1981.

Reprint requests

Dr. Oguz Ozcelik, Fırat University Faculty of Medicine (Tip Fak) Department of Physiology, Elazig, Turkey, E-mail: oozcelik@excite.com