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Original Article

How effective is the obesity treatment on improving oxidative stress? Is there any difference between drugs?

Obezite tedavisi oksidatif stresi düzeltmede ne kadar etkili? İlaçlar arasında fark var mı?

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ABSTRACT

Introduction: Obesity shortens the life period and decreases its quality, causing several complications. Recently, oxidative stress produced by lipid peroxydation is considered a cardiovascular risk factor. In this study, we aimed to investigate the relationship between weight loss with lipid profile, insulin resistance, and lipid peroxidation products malondialdehyde (MDA, oxidant) and paraoxonase-1 (PON1, antioxidant) levels which is protective in atherosclerosis, and to evaluate alteration on oxidative stress.

Methods: Patients diagnosed as obese at the Endocrinology and Metabolic Diseases Outpatient Clinics of Inonu University Faculty of Medicine between December 2005 and February 2008 were studied. 103 patients were included in the study. Study population was divided into two treatment groups. In the first group, 120 mg of orlistat, three times daily, and in the second group, sibutramine 15 mg per day were given in addition to appropriate diet therapy. The patients were evaluated at the end of three months treatment period.

Results: Dramatic changes in body weight, Body Mass Index (BMI), and waist and hip circumference were observed during the three-month evaluation in patients receiving orlistat or sibutramine. Additionally, significant improvements were measured in systolic-diastolic blood pressure levels, lipid levels, and insulin resistance. The decrease in the MDA level and the increase in the PON level were similar and significant in both patient groups.

Discussion and Conclusion: The treatment of obesity, aimed at reducing body weight, acts to reduce oxidative stress by increasing paraoxonase-1 activity (antioxidant) and reducing the amount of the peroxidation product malondialdehyde (oxidant), regardless of the type of medication administered.

Keywords: Malondialdehyde, obesity, orlistat, paraoxonase, sibutramine

ÖZ

Giriş ve Amaç: Obezite; neden olduğu pek çok komplikasyon nedeniyle hem yaşam süresini kısaltır hem de kalitesini azaltır. Mortaliteyi artıran en önemli komplikasyonlar kardiyovasküler sistem ile ilgili olanlardır. Son zamanlarda lipid peroksidasyonu sonucu oluşan oksidatif stres kardiyo-vasküler bir risk olarak kabul edilmektedir. Çalışmamızda kilo kaybı ile lipid profili, insülin direnci, peroksidasyon ürünü malondialdehit (MDA-oksidan) ve aterosklerozda koruyucu rol üstlendiği bildirilen Paraoksonaz-1 (PON1-antioksidan) düzeyleri arasındaki ilişkiyi araştırmayı ve böylece oksidatif stresteki değişimi belirlemeyi amaçladık.

Yöntem ve Gereçler: 2005 yılı Aralık ayı ile 2008 Şubat ayı arasında İnönü Üniversitesi Tıp Fakültesi Turgut Özal Tıp Merkezi Endokrinoloji ve Metabolizma Hastalıkları Polikliniğine obezite nedeniyle başvuran hastalar çalışma için ön değerlendirmeye alındı. Çalışmaya toplam 103 hasta alındı. Karaciğer ve böbrek fonksiyon testleri anormal olan hastalar çalışmaya alınmadı. Hastalar uygun diyetle beraber iki gruba ayrıldı. Orlistat 3x120 mg ve sibutramin 1x15 mg verildi. Üçüncü ay kontrolleri değerlendirildi.

Bulgular: Orlistat ve sibutramin ilaç tedavisi alan hastaların başlangıç ve 3. ay kontrollerindeki kilo, beden kitle indeksi, bel, kalça çevresi değerlerinde anlamlı

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değişiklikler tespit edildi. İlave olarak sistolik-diastolik basınç, lipid düzeyleri, insülin direnci üzerindeki anlamlı düzelmeler tespit edildi. Oksidan (MDA) düzeyinde azalma ve antioksidan (PON) düzeylerinde artış her iki ilaçta da benzer ve anlamlı idi.
Tartışma ve Sonuç: Antiobezite tedavisi ile sağlanan kilo kaybı; kullanılan ilaçlardan bağımsız olarak peroksidasyon ürünü malondialdehit (oksidan) düzeylerini azaltıp paraoksonaz-1 (antioksidan) düzeylerini artırarak oksidatif stresi azaltmaktadır.

Anahtar kelimeler: Malondialdehid, obezite, orlistat, paraoksonaz, sibutramine

INTRODUCTION

Obesity; it is a chronic disease with an increasing prevalence in the world and increasing adipose tissue-derived morbidity (diabetes mellitus, hypertension, dyslipidemia, heart disease, stroke, sleep apnea, and cancer) and causes a significant increase in mortality. The most important reason here is the presence of chronic inflammation together with oxidative stress. In addition, insulin resistance triggers prooxidant and proinflammatory mechanisms and increases the progression of atherosclerosis (1,2). It is a known fact that there is a significant decrease in obesity-related morbidity with weight loss (3,4).

The fact that obesity carries a potential risk of morbidity and mortality makes it imperative to seriously address its treatment. To this end, exercise and low-calorie diets are used first, and in cases where this is not sufficient, additional medications are used (5). Sibutramine; It increases central sympathetic activity and reduces food intake with its appetite-reducing effect. On the other hand, orlistat does not cause significant systemic absorption in the gastrointestinal tract, inhibits lipase release, and reduces fat absorption (6). Antiobesity drug therapy helps weight loss and reducing lipid levels, which leads to positive changes. As a result, lipid peroxidation and antioxidation changes can reduce cardiovascular risk. For this reason, we aimed to examine the lipid profile and oxidation marker malondialdehyde acid (MDA), which changes with weight loss, and the paraoxonase -1 (PON-1) level, which is reported to play a protective role in atherosclerosis. For this reason, we aimed to examine the lipid profile that changes with weight loss, the oxidation marker malondialdehyde acid, and the paraoxonase -1 level reported to play a protective role in atherosclerosis.

MATERIALS AND METHODS

Inclusion criteria

In our study, the patients diagnosed as obese at Endocrinology and Metabolism Diseases Outpatients Clinics of Inonü University Faculty of Medicine between December December 2005 and February 2008 had normal liver and kidney functions and had a body mass index (BMI) above 30 kg/m^2 were included.

Exclusion criteria

Patients with unexplained tachycardia (over 100 beats/min) and arrhythmia, hypothyroidism, hyperprolactinemia, Cushing syndrome, any of the congenital syndromes with secondary obesity, chronic liver disease, chronic kidney failure, ischemic heart disease, heart valve disease, advanced heart failure, malignant disease, liver enzyme levels above twice the upper limit, neurological and psychiatric diseases, those receiving hormone replacement therapy and steroid therapy, who had gastroplasty those who had an intestinal by-pass operation, those who were planning to become pregnant, breastfeeding mothers, and those who received treatment for weight loss in the near future were not included in the study.

The study protocol was approved by the Inonu University Faculty of Medicine Ethics Committee with decision number 2005/91 (December 2015) and was conducted in accordance with the revised principles of the Declaration of Helsinki. Patients were informed about the study, the treatment, and the medications that would be used, and their consent was obtained. The study was planned as an open, parallel study without a control group. Group 1; orlistat 3x120 mg (three times a day at each meal, in the first bite of a meal), Group 2; it was created by giving sibutramine 15 mg 1x1 (at the first meal in the morning, with an empty

stomach). Detailed medical histories and system queries of the patients were recorded.

Evaluation of measurements

Detailed systemic physical examinations were performed by measuring height, weight, pulse rate, arterial blood pressure, and waist and hip circumferences. These evaluations were repeated at each control period.

Both spinae iliaca posterior are measured superiorly and at the narrowest point crossing through the navel while the person is standing (over 102 cm for men and 88 cm for women indicates cardiovascular risk). Hip circumference measurement was made by joining the symphysis pubis point from the widest part of both hips. Waist/hip ratio (WHR) was calculated (waist/hip ratio above 0.9 in men and 0.85 in women indicates cardiovascular risk). BMI>30kg/m^2 was taken as a criterion for the diagnosis of obesity. For this, the constant bioelectricity in the Endocrinology Polyclinic Impedance device (TANITA-Body Composition Analyzer Type TBF-300 M Tokyo JAPAN) was used.

Diet and exercise regulation

After the diagnosis of obesity, patients are consulted by a nutritionist, and their dietary intake was adjusted as 55-60% of the daily requirement suitable for their ideal weight is carbohydrates, 25-30% protein, and 10-15% fat. It is recommended that they take a regular walk for 1 hour a day. Three months after starting the diet, patients were divided into two groups and one group received orlistat (group 1); 120 mg three times daily just before each meal, 15 mg once daily on an empty stomach in the morning meal, in the other group was started on sibutramine (group 2). Physical and laboratory changes of the patients were re-evaluated in the 3rd month of drug treatment.

Laboratory examinations were evaluated by centrifuging venous blood samples from the ante-cubital region at 3750 rpm for 10 minutes in a gel biochemistry tube between 08.30 and 09:00 in the morning, following a 12- hour fasting at the beginning of the study and during the control period (3rd month of the treatment). Fasting blood glucose (mg/dl) and postprandial blood glucose taken two hours after the meal (mg/dl) based on hexokinase method (Enzymatic UV test) Olympus AU 2700 (Olympus Diagnostics GmbH, Hamburg, Germany) device. Then insulin levels were measured with a chemiluminescent -based Immulite 2000 system (DPC, CA, USA). Total cholesterol (mg/dl), HDL-cholesterol (mg/dl), LDL-cholesterol (mg/dl), triglyceride (mg/dl), uric acid (mg/dl), alanine aminotransferase (ALT, U/L), aspartate aminotransferase (AST, U/L), blood urea nitrogen (BUN, mg/dl), creatinine (mg/dl), insulin (uIU/mL), C peptide (ng/mL), high sensitive C-reactive protein (hs-CRP) (mg/L), fibrinogen (mg/dl), lipoprotein a (g/L) were measured by photometric method (Olympus Diagnostics GmbH, Hamburg, Germany). HOMA-IR (Homeostasis Model Assessment-Insulin Resistance) is used to measure patients' insulin resistance. For this; Fasting serum insulin x Fasting plasma glucose (mg/dl) / 405 formula was used.

Paraoxonase and Malondialdehyde Activity Biochemical Measurements

Venous blood taken into a normal biochemistry tube with gel was centrifuged at 3750 rpm for 10 minutes, and serum samples were separated and stored at -70 ^{0} C until the day of the study.

Chemical Ingredients

1,1,3,3- tetraethoxypropane trichloroacetic acid and p-nitrophenol were obtained from Sigma (St Louis, MO, USA), and all other chemicals were obtained purely from different companies.

Reagents

PON reagent: 15.98 g Tris-base (0.132 mmol /L), 0.146 g CaCl2 (1.32 mmol /L) and 153.7 g NaCl (2.63 mmol / L) were weighed. The volume was made up to 1 L by adjusting the pH to 7.8. MDA Reagent: 0,65 g of thiobarbituric acid was dissolved in 100 ml of distilled water by heating.

Methods

PON activity determination: PON enzyme activity was determined by hydrolysis of p-nitrophenol. Accordingly, test tubes were prepared by adding 200 µl of p-nitrophenol (5.5 mmol / L) to 1000 µl of PON reagent. 10 µl of a serum sample from patient samples was added to the medium, mixed rapidly and placed in the spectrophotometer. absorbance was monitored at 405 nm at 25 °C for 3 minutes. Molar by taking ΔA of the results multiplied by the extinction coefficient (€= 18.05 x 10^{-3}) and expressed in U/L. All patient samples were studied twice (7,8).

Malondialdehyde determination: Malondialdehyde measurement was determined by the method of Yagi et al.[10] Accordingly, 500 µl of serum sample was mixed with the thiobarbituric acid reagent. Then it was boiled together for 30 minutes in a water bath of 100 °C.4 ml of n-butanol was added to the tubes, cooled under cold water, and vortexed for 10 minutes. The absorbance of the pink color formed in the upper phase of the liquid was measured at the end of the extraction process using a spectrophotometer at a wavelength of 532 nm. T results were determined using the 1,1,3,3-tetraethoxypropane standard and expressed in nmol/mL of serum (9,10).

Statistics evaluation

Statistical analyzes were performed with SPSS for Windows version 13.0 (SPSS Inc., Chicago, Illinois, USA). Whether the data showed normal distribution or not was evaluated with the Kolmogorov-Smirnov test. Mann-Whitney U and Unpaired t tests were used to compare continuous variables. The Chi-square test was used to compare categorical variables. P<0.05 values were considered statistically significant.

RESULTS

A hundred and three patients aged between 25-60 years were included in the study. Of the patients, 14 (13.6%) were male, and 89 (86.4%) were female. The anamnesis of the patients was evaluated at the time of admission to our outpatient clinic. It was determined that 18 patients (17.5%) had diabetes mellitus, 12 patients (11.5%) had alcohol use and 26 patients (25.2%) had hypertension. The patients who will be treated with orlistat and sibutramine are respectively; divided into group 1 and group 2. There was no difference between the mean age and BMI in the baseline period of both groups, and their values are given in Table 1.

Table 1. The mean age and BMI of the patients at baseline.

	Orlistat (n=52)	Sibutramine (n=51)	Total (n=103)
Age(years)	47.32±10.64	41.29±8.22	44.3± 9.94
BMI (kg/m^2)	38.20± 5.94	37.30± 5.11	37.76± 5.54

BMI: Body mass index

Sibutramine treatment group, 35 (68.6%) were obese and 16 (31.4 %) were morbidly obese. Of the patients who received orlistat treatment, 35 (67.3%) were obese and 17 (32.7) were morbidly

Table 2. Baseline and control anthropometric changes of groups 1 and 2.

	Orlistat (n=52)			Sibutramine (n=51)		
	Beginning	3rd month	p value	Beginning	3rd month	p value
weight (kg)	96.18±15.73	84.52±14.95	<0.01	95.38±13.24	85.00±15.41	<0.01
BMI (kg/m^2)	38.20±5.94	33.55±5.60	<0.01	37.30±5.11	33.28±6.09	<0.01
Waist circumference (cm)	124.40±20.19	95.42±11.27	<0.01	117.21±16.57	93.78±10.27	<0.01
Hip circumference (cm)	137.90±13.35	113.46±11.91	<0.01	129.27±12.52	105.86±10.88	<0.01
WHR	0.90±0.10	0.83±0.14	<0.05	0.90±0.08	0.88±0.09	NS

**Not Significant (NS) (p>0.05), BMI: Body mass index, WHR: Waist/hip ratio*

obese. There were statistically significant changes in weight, BMI, waist, and hip circumferences compared to the baseline values of both groups in the 3rd month of antiobesity treatment. While the decrease in waist hip ratio (WHR) at the third month was significant in the orlistat group, it was not statistically significant in the sibutramine group. The anthropometric changes of the patients at baseline and 3rd month follow-ups are summarized in Table 2. Chart 1 shows the baseline and 3rd-month control weight and BMI changes in both groups.

For fasting insulin levels; a significant decrease were observed in both groups between the baseline values and the 3rd month control values in all patients ($p<0.001$) (Table 3). The HOMA-IR formula was used to measure the patients' insulin resistance, and the value of >2.7 was considered insulin resistance. Insulin resistance was present at baseline in 89 patients (86.4%). In both groups, insulin resistance was found to be significantly lower than at the start of treatment ($p<0.001$).

A significant decrease was observed in the patients' total cholesterol levels in groups 1 and 2 at admission and 3rd-month controls (Table 4).

While HDL-cholesterol values were significantly increased in group 1 ($p<0.01$), there was a decrease in HDL values in group 2. However, this decrease was not statistically significant. When the reference values of LDL-cholesterol levels were compared with the 3rd month control values, a statistically significant decrease was found in both drugs. However, this decrease was statistically more significant in group 1 compared to group 2 ($p<0.01$, $p<0.05$, respectively).

The most marked decreased lipid type in patients using orlistat was triglyceride. There was a decrease in triglyceride levels between the baseline values and the 3rd month controls in both groups, but it was not significant in the sibutramine group. When the fibrinogen, hs-CRP, and lipoprotein (a) levels of the patients were compared, there were statistically significant

Table 3. Control blood glucose, insulin and HOMA-IR values at 3 months of treatment.

	Orlistat			Sibutramine		
	Beginning	**3rd month**	**p value**	**Beginning**	**3rd month**	**p value**
HbA1c (%)	6.73±2.05	5.92±1.15	<0.01	6.01±1.01	5.44±0.66	<0.01
FPG (mg/dl	128.34±62.94	102.71±27.47	<0.01	108.64±29.82	96.11±14.77	<0.01
PPG (mg/dl)	150.98±76.91	122.38±43.60	<0.01	135.82±51.78	111.21±27.30	<0.01
Insulin (uIU/mL)	17.07±9.12	12.44±4.12	<0.01	17.02±7.90	12.78±5.08	<0.01
HOMA-IR	5.47±4.02	3.16±1.35	<0.01	4.65±2.86	3.06±1.39	<0.01

FPG: Fasting plasma glucose, PPG: Post prandial glucose, HOMA-IR: Homeostasis Model Assesment-Insulin Resistance

Table 4. Evaluation of lipid and acute phase reactants in the 3rd month controls of antiobesity treatment.

	Orlistat			Sibutramine		
	Beginning	**3rd month**	**p value**	**Beginning**	**3rd month**	**p value**
TG (mg/dl)	199.07±111.44	149.55±81.76	<0.01	160.13±95.62	143.58±73.79	NS
Total chol (mg/dl)	200.71±39.24	178.80±39.50	<0.01	198.52±45.91	187.23±36.50	<0.05
LDL-chol (mg/dl)	127.17±32.49	101.67±29.86	<0.01	122.23±40.97	106.72±25.24	<0.05
HDL-chol (mg/dl)	45.62±8.81	48.7±8.78	<0.01	51.28±12.00	50.35±8.73	NS
VLDL-chol(mg/dl)	39.33±22.50	34.99±24.48	NAME	31.61±15.98	33.56±19.48	NS
Fibrinogen(mg/dl)	330.63±102.17	295.23±105.20	<0.01	328.13±103.01	325.88±126.57	NS
hs-CRP	6.44±4.45	4.18±3.11	<0.01	6.77±5.36	4.44±3.11	<0.01
Lipo (a)(g/L)	0.38±0.52	0.17±0.28	<0.01	0.33±0.42	0.20±0.24	<0.01

TG: triglyceride (mg/dl), Total chol: Total cholesterol (mg/dl), LDL-chol: Low density lipoprotein- cholesterol (mg/dl), HDL- chol: High density lipoprotein cholesterol (mg/dl), VLDL- chol: Very low density lipoprotein-cholesterol(mg/dl), high sensitive C-reactive protein (hs-CRP) (mg/L), Lipo(a): Lipoprotein a (g/L)

Table 5. MDA and PON values at 3 months of treatment.

	Orlistat			Sibutramine		
	Beginning	3rd month	p value	Beginning	3rd month	p value
MDA (nmol/mL)	4.66±1.37	3.53±1.11	<0.01	4.72±1.76	3.78±1.49	<0.01
PON (U/l)	175.27±67.79	198.15±62.20	<0.01	172.98±63.75	199.39±58.03	<0.01

MDA: Malondialdehyde acid, PON: Paraoxonase

decreases in group 1 (p<0.01), but the decrease in fibrinogen in group 2 was not significant in the 3rd-month controls from admission.

When the MDA levels of the patients were compared, a statistically significant decrease was found in the initial and 3rd-month control values of both drugs. In contrast, a statistically significant increase was found in the serum PON levels (Table 5).

The decrease in MDA and increase in PON levels were similar in both drugs, and there was no statistically significant difference between the two groups (Table 6).

Table 6. MDA and PON difference values at the 3rd month control.

	Orlistat (n=52)	Sibutramine (n=51)	p value
MDA difference	1.12±1.29	0.94±1.13	NS
PON difference	22.87±41.69	26.41±32.44	NS

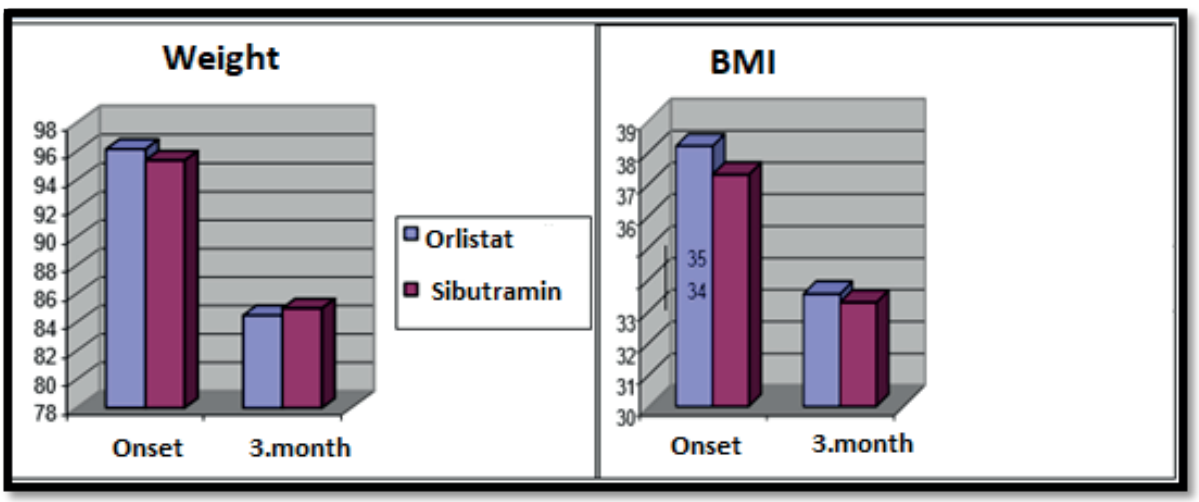
MDA: Malondialdehyde acid, PON: Paraoxonase

Side effects of drugs

Diarrhea and greasy stool were the most common adverse events in the group receiving orlistat therapy throughout the study (n=30, 57.69%). However, these side effects have become tolerable with the appropriate diet (low in fat). In the group receiving sibutramine treatment, dry mouth was the most common side effect (n=20, 39.21%). In addition, constipation (n=30, 58.82%), irritability (n=10, 19.60%), insomnia (n=6, 11.76%) were observed in this patient group. When the patients in both groups were questioned, it was determined that they had complaints at a level that could tolerate the drug, and the treatment was not discontinued because of these side effects.

DISCUSSION

It is known fact that obesity causes inflammation at the cellular level and causes free radical formation. Again, obese adipose tissue is characterized by inflammation, and progressive



Graphic 1. Onset and 3. month control weight and BMI change.

inflammation promoted by macrophages has been demonstrated. There is a significant relationship between the production of proinflammatory cytokines called adipokines and the metabolic complications of obesity (such as C-reactive protein, fibrinogen, lipoprotein a). Lipid peroxidation products accelerate this atherogenesis.

Hyperinsulinemia causes cellular LDL oxidation independent of impaired glucose tolerance and lipid levels. These increased levels of oxidized LDL carry cardiovascular risk due to significant cell necrosis of myocardium and increase the risk of ischemia (11).

Adipose tissue has long been recognized as a major source of inflammation and oxidative stress products. MDA is a key oxidative stress product produced by peroxidation that has been reported to be considerably greater in obese persons (12). Various studies have been conducted to evaluate the effect of weight loss on oxidative stress. Among these, Yeşilbursa et al.[13] conducted a comparative study of 36 obese patients with 11 healthy control patients and compared the weight, BMI, blood lipid, and MDA values before orlistat treatment and at the 6th-month controls. MDA levels were statistically significant and higher in obese patients compared to the healthy control group at the beginning. After 6 months, the control's mean weight loss was 6.8 kg, and the decrease in BMI was 3.2 kg/m^2. MDA level decreased from 2±0.77 to 0.89±0.41 nmol/mL; this difference was statistically significant ($p<0.001$). A positive correlation was found between MDA level and BMI in the 6th-month controls ($r=0.6$, $p<0.0001$). In our study, similar results were obtained with orlistat and sibutramine treatment, and a significant decrease was found in BMI, weight loss, and MDA levels.

Özkan et al.[14] conducted a study on 30 obese patients. After 3 months of orlistat treatment, a significant weight loss was achieved compared to the baseline ($p<0.05$) along with a significant decrease in serum total cholesterol, LDL cholesterol, and triglyceride levels and an increase in HDL-cholesterol. A significant increase was observed compared to pre-treatment. Our study was similar in the group of patients who received orlistat treatment, with significant changes in weight loss and a significant contribution to the lipid profile. However, MDA levels showed a significant decrease compared to pre-treatment levels.

Paraoxonase, on the other hand, is an important antioxidant enzyme associated with HDL-cholesterol and can hydrolyze oxidized lipids in the body (15). Previous studies have also shown that PON, which is closely related and associated with HDL, plays an important role in preventing atherogenic development by preventing LDL oxidation in the body. In a multicenter, randomized study by Audikovszky et al.[16], 139 obese patients were divided into two groups. Treatment of the first group (78 obese patients) was supplemented with a suitable diet and 3x120 mg orlistat for six months. In the second group, six months of follow-up made with only the appropriate diet. At the end of the sixth month, there were statistically significant decreases in weight, BMI, and waist circumference in the 1st group using orlistat compared to the diet group. A decrease in fasting blood sugar, blood pressure, cholesterol, and triglyceride levels was also observed in the patient group using orlistat. In addition, a significant increase was found in serum PON1 activity compared to the diet group. In our study, a significant improvement in lipid profile in the 3rd-month controls of patients using orlistat supports an increase in antioxidant capacity (PON-1) together with a decrease in oxidant capacity.

Numerous studies have shown that obesity (as an independent risk factor) is one of the most important determinants of cardiovascular risk factors (17). Data obtained in the Framingham

study revealed that obesity is an independent risk factor for coronary artery disease (CAD) (18-20). It is also associated with many other risk factors such as high blood pressure, hypercholesterolemia, low HDL-C, high triglycerides, and diabetes mellitus (21-24).

Aged of 45-54 participated, and cardiovascular disease was evaluated in patients with BMI > 29 kg/m^2. Of mortality, it has been reported that it increased 2 times compared to the control group and 4 times in those with BMI > 32 (25). In another study, it was reported that there was an increase in death rates due to cardiovascular causes when BMI > 30 (26). With a 10% body weight loss, a 50% decrease in risk occurs (27).

Varol et al.[28] investigated the effect of orlistat on plasma lipid levels with short-term (1 month) treatment in 13 obese patients. While the initial BMI was 33.4±1.6 in treatment, it was found to be 33.3±1.5 after 1 month of treatment, and this change was not statistically significant (p=0.2). In contrast, there was a statistically significant decrease (p<0.05) in total cholesterol, triglyceride, LDL cholesterol, and fasting blood glucose levels evaluated after treatment, the increase in HDL cholesterol level was not considered significant (p=0.09).

CONCLUSION

In the light of these findings, in our study, significant changes in weight loss were achieved with 3-month orlistat and sibutramine treatment in obese patients. In addition, a significant improvement was achieved in lipid and oxidant levels, while a significant contribution was made to the increase in antioxidant capacity. As a result, it has an important place in reducing cardiovascular risks, which are important causes of morbidity and mortality in obesity. This change in weight loss; has an effective and important role in the prevention of atherosclerosis.

Ethics Committee Approval: The study protocol was approved by the Inonu University Faculty of Medicine Ethics Committee (2005/91).

Conflict of Interest: The authors have declared that they have no conflict of interest.

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