Turkish Journal of Endocrinology and Metabolism, (2004) 1 : 35-42 **ORIGINAL ARTICLE**

Effects of Sibutramine Use on Weight, Body Mass Index, Waist / Hip Ratio, and Blood Lipid Parameters, Compared to Placebo, in Obese Individuals

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Worldwide obesity is a chronic condition that is characterized by accumulation of extra fat in the body and that results in increased mortality and morbidity. The aim of the present study is to evaluate the effects of sibutramine, an anorectic medication, on body weight, body mass index (BMI), waist/hip ratio and blood lipid parameters in obese individuals.

The study enrolled 58 obese patients (54 female and 4 male) whose BMI was > 30 and mean age was 40.53 ± 10. The patients were allocated to two groups. Group I was administered sibutramine 10 mg / day (n=30) and Group II received placebo (n=28). In addition, the two groups were given a calorie-restricted diet apart from their treatments. Body weights, BMI, waist/hip ratios, serum lipids, blood pressures and heart rates of enrolled patients were measured before the treatment and after 12 weeks of treatment. Echocardiographic evaluation was also made.

At the end of study, body weights of sibutramine group and placebo group decreased significantly, compared to pretreatment (for each group p level <0.05), but no statistically significant difference was observed between the two groups. BMI decreased both in sibutramine group ($p<0.05$) and placebo group ($p<0.05$). Waist/hip ratio decreased in sibutramine group ($p<0.05$) but did not change in placebo group. Total cholesterol, LDL-cholesterol and triglyceride values decreased (for each of them $p<0.05$), but HDL-cholesterol increased ($p<0.05$). Total cholesterol, LDL-cholesterol and triglyceride values did not significantly change in the placebo group; however HDL-cholesterol increased slightly ($p>0.05$). Systolic blood pressure ($p<0.05$) and heart rate ($p<0.05$) decreased in obese patients given sibutramine, but increased significantly in the placebo group. Recently developed valvular heart disease and pulmonary hypertension were not identified by echocardiography in sibutramine group or placebo group during treatment.

In conclusion, we observed that low-calorie diet and 10 mg/day sibutramine use were more effective than placebo in weight loss. However, when we compared the amount of weight loss we could not observe any significant difference. Moreover we concluded that sibutramine affected lipid parameters favorably, was not associated with very important complications that could lead to discontinuation and did not have any negative effect on heart valves.

Key words: **Obesity, Sibutramine**

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Introduction

Obesity is a condition, which occurs as a result of increased fat tissue percentage in the body. Despite important advances in science and technology,

increased economic power and elimination of major health problems related to under nutrition, excessive food intake and energy surplus have led to new health concerns (1).

Obesity is a systemic condition which may lead to type 2 diabetes mellitus (Type 2 DM), hypertension, atherosclerotic heart disease, cerebrovascular diseases and respiratory system problems, gall bladder diseases, some cancer forms, musculo-articular conditions and many other problems (2).

Since obesity involves multiple body systems, results in problems, impairs quality of life, decreases life expectancy and imposes a heavy economic burden on patients, it is now considered as a condition that should be treated (2-4). Number of obese individuals is progressively increasing and obesity is seen as a reason for increased morbidity and mortality (3).

Physical, metabolic, endocrinologic and psychological complications may be diminished by weight loss in obese individuals and obesity related mortality may decrease (2, 5). Sibutramine is a centrally acting drug used in the treatment of obesity. It inhibits serotonin (5-HT) and noradrenaline (NA) reuptake in a dose dependent manner (6,7). The aim of this study is to evaluate the effect of sibutramine, an anorectic medication, on body weight, BMI, waist/hip ratio and blood lipid parameters, compared to placebo, in obese individuals.

Materials and Method

The study enrolled 58 individuals who were admitted to Endocrinology outpatient clinic in Fırat Medical Center at Fırat University (aged between 20-60 years [mean age: 40.53 ± 10.31 years], BMI > 30) with a concern about obesity and wished to lose weight. Obese patients enrolled in the study were divided into two groups: sibutramine group (n=30 patients; 28 female and 2 male) and placebo group (n=28 patients; 26 female and 2 male). Grouping was made in a randomized fashion. Patients were informed about how the study will be conducted and properties of the drug they will use. Patients gave informed consent and study was approved by the Ethics Committee of Fırat University.

Patients with hypertension that could not be controlled with medication (blood pressure could not be decreased to <150/95 mm Hg); patients having unexplained tachicardia and arrhythmia Type 1 diabetic patients, patients having obesity related to hypothyroidism, Cushing syndrome or any congenital syndrome; patients with a diagnosis of chronic pulmonary disease, chronic renal insufficiency, ischemic heart disease, valvular heart disease, advanced heart failure; patients having liver enzymes 2 x upper the normal limit; patients with major neurological or psychiatric diseases; patients on hormone replacement therapy and steroid therapy; patients who had undergone gastroplasty and intestinal by-pass procedures for weight loss; women who have a possibility of pregnancy or plan to be pregnant, lactating mothers, patients recently given medical therapy for weight loss and lost more than 3 kgs in the past 3 months; patients over 69 or under 19 years of age, patients with a condition that would preclude their participation in the follow-up visits and patients having a condition that would preclude their compliance with the assigned diet were excluded from the study.

A comprehensive history about obesity and related problems were obtained from the enrolled individuals. Concurrent illnesses and concomitant drug use were sought. Familial predisposition and reasons predisposing obesity were assessed.

Physical examination was performed. Body weights and heights of patients were measured to calculate BMI. Waist circumference was measured while the patient was standing with clothes taken off (only underwear). Measurement was made at a level between lower edges of the ribs and crista iliacas after a normal expiration. Hip circumference was measured with a measure and waist/hip ratio (WHR) was calculated. The same person performed all measurements with the same balance and measure in order to decrease the error possibility.

Whole blood count and biochemical parameters were measured by AU600 autoanalyzer. Electrocardiography was performed in order to assess ischemic heart disease and arrhythmia. ATL-Ultramac echocardiography was performed to assess valvular heart disease and pulmonary hypertension.

A standard oral glucose tolerance test (OGTT) was carried out in two groups by 75 g glucose before and after the treatment in obese, but not diabetic patients. Any blood glu cose value ≥200 mg/dL in

the 1st and the 2nd hour was defined as diabetes. Impaired OGTT was considered at levels of 140-200 mg/dL.

This study was single-blind. Medication group received sibutramine hydrochloride monohydrate (Reductil® 10 mg), a selective serotonin and noradrenaline reuptake inhibitor, and placebo group received placebo with an identical appearance. Reductil and placebo were given as a single oral dose 1-2 hours before breakfast.

Both groups were given calorie-restricted diet for weight loss. When measuring the amount of calories to be lost, their normal body weight corresponding to their height was calculated and 24 calories/kg diet was administered. While administering the diet to hypertensive and diabetic patients, their conditions were considered. Individuals were instructed to comply with their diet as far as possible. Diet was rendered enjoyable by giving diverse diet lists.

Individuals enrolled were given advises about physical exercise that they could perform without much stress.

The study lasted for 12 weeks with the control visits performed every 4 weeks. At these follow-up visits compliance with the diet and exercise recommendations and complaints about the treatment were assessed. At the end of the 12-week therapy, all the parameters initially measured were checked. Paired sample t-test was used to evaluate whether there was a significant difference between pretreatment values and values after 12 weeks of therapy. The lowest significance level was considered as $p<0.05$. All the values were expressed as mean ± standard deviation.

Results

Although initially 65 obese individuals were enrolled, 7 of them discontinued for various reasons. A total of 58 obese individuals completed the 12-week study. Obese patients were 20-60 years of age (mean age: 40.53 ± 10.31 years). Of those who completed the study, 54 individuals were female (93.1%) and 4 were male (6.9%). 34 patients received sibutramine plus calorie restricted diet and 24 patients placebo plus calorie restricted diet.

Patients in the sibutramine group were 20-58 years old (mean age: 41.47 ± 9.9 years) and there were 32 female patients (94.12%) and 2 male patients (5.88%). Patients in the placebo group were 20-60 years old (mean age: 39.20 ± 10.93 years) and there were 22 female patients (91.67%) and 2 male patients (8%). Female/male ratios were similar in both groups. There was no significant difference in terms of mean age and sex between the two groups.

Eight patients had hypertension (23.53%) and 3 patients had diabetes mellitus (8.82%) in the sibutramine group. In the placebo group 5 patients had hypertension (20.83%) and 2 patients had diabetes mellitus (8.33%). 26 patients (76,47%) in the sibutramine group and 20 patients (83.33 %) in the placebo group reported that there was at least one obese individual in their families. 15 patients in the sibutramine group (44.11%) and 8 patients in the placebo group (23.33%) reported that there was at least one individual with Type 2 diabetes mellitus in their families.

Obese patients without diabetes had OGTT with 75 g glucose. Glucose intolerance was found in 9 patients in the sibutramine group (29.03%) and 4 patients in the placebo group (18.18%).

Age, height, body weight, BMI, WHR, systolic and diastolic blood pressures and pulse rates of obese individuals enrolled are shown in Table 1. Baseline body weight, BMI, systolic and diastolic blood pressures and pulse rates were not different in the two groups. There was a significant difference between baseline WHR of sibutramine group (0.88 ± 0.06) and that of placebo group (0.84 ± 0.05) ($p<0.05$).

Total cholesterol, LDL-cholesterol and triglyceride values decreased (for each of them $p<0.05$), but HDL-cholesterol increased ($p<0.05$). Total cholesterol, LDL-cholesterol and triglyceride values did not significantly change in the placebo group; however HDL-cholesterol increased slightly ($p>0.05$). Systolic blood pressure ($p<0.05$) and heart rate ($p<0.05$) decreased in obese patients given sibutramine, but increased significantly in the placebo group. Recently developed valvular heart disease and pulmonary hypertension were not identified by echocardiography in sibutramine group or placebo

Table 1. Basal age, height, body weight, BMI, WHR, systolic, diastolic blood pressures and pulse rates values of obese individuals.

Parameters	Sibutramin (n = 34)	Placebo (n = 24)	Student's t test
Age (years)	41.47 ± 9.9	39.20 ± 10.93	p>0.05
Height (cm)	155.66 ± 15.92	155.95 ± 6.49	p>0.05
Weight (kg)	97.66 ± 15.92	92.60 ± 13.77	p>0.05
BMI (kg / m^2)	40.73 ± 7.10	38.24 ± 6.52	p>0.05
WHR	0.88 ± 0.06	0.84 ± 0.05	P<0.05
SBP (mmHg)	125.29 ± 18.98	120.62 ± 18.07	p>0.05
DBP (mmHg)	83.52 ± 11.64	78.58 ± 18.68	p>0.05
Pulse Rate (minute)	80.41 ± 7.33	79.33 ± 9.14	p>0.05

BMI = Body Mass Index, WHR = Waist / Hip Ratio, SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure

Tab le 2. Changes from pretreatment to 12 weeks after the treatment in parameters of body and biochemical parameters of blood in sibutramine group.

Biochemical Parameters	Before treatment (n = 34)	After treatment (n = 34)	Student's t test
Weight (kg)	97.66 ± 15.92	88.36 ± 15.97	p<0.05
BMI (kg/m^2)	40.73 ± 7.10	36.62 ± 6.90	p<0.05
WHR	0.88 ± 0.06	0.87 ± 0.05	P<0.05
SBP (mmHg)	125.29 ± 18.98	128.23 ± 25.27	p>0.05
DBP (mmHg)	83.52 ± 11.64	83.08 ± 14.87	p>0.05
Pulse Rate (minute)	80.41 ± 7.33	84.64 ± 6.88	P<0.05
AST (U/l)	24.91 ± 7.32	22.50 ± 6.98	p>0.05
ALT (U/l)	26.52 ± 10.90	24.32 ± 8.84	p>0.05
Urea (mg/dl)	24.20 ± 6.24	25.50 ± 7.08	p>0.05
Creatinine (mg/dl)	0.81 ± 0.14	0.89 ± 0.16	p>0.05
T. Cholesterol (mg/dl)	211.94 ± 43.07	193.35 ± 35.57	p<0.05
HDL-cholesterol (mg/dl)	41.00 ± 8.54	50.08 ± 10.66	p<0.05
LDL-cholesterol (mg/dl)	130.88 ± 36.86	120.32 ± 30.58	p<0.05
TG (mg/dl)	198.85 ± 83.40	137.91± 43.65	p<0.05

BMI = Body Mass Index, WHR = Waist / Hip Ratio, SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure, AST = Aspartate aminotransferase ALT= Alanine aminotransferase, T. Cholesterol = Total cholesterol, HDL-cholesterol = High Density cholesterol, LDL-Cholesterol= Low Density Cholesterol, TG = Triglyceride

Table 3. Changes from pretreatment to 12 weeks after the treatment in parameters of body and biochemical parameters of blood in placebo group.

Biochemical Parameters	Before treatment (n = 24)	After treatment (n = 24)	Student's t test
Weight (kg)	92.60 ± 13.77	87.33 ± 13.42	p<0.05
BMI (kg/m2)	38.24 ± 6.52	35.98 ± 6.46	p<0.05
WHR	0.84 ± 0.05	0.83 ± 0.05	p>0.05
SBP (mmHg)	120.62 ± 18.07	122.29 ± 16.68	p>0.05
DBP (mmHg)	78.58 ± 18.68	78.95 ± 10.63	p>0.05
Pulse Rate (minute)	79.33 ± 9.14	77.25 ± 8.86	p>0.05
AST (U/L)	21.87 ± 5.22	22.45 ± 6.38	p>0.05
ALT (U/L)	21.79 ± 9.18	22.66 ± 8.37	p>0.05
Urea (mg/dl)	25.87 ± 6.02	27.37 ± 7.55	p>0.05
Creatinine (mg/dl)	0.85 ± 0.15	0.87 ± 0.10	p>0.05
T. Cholesterol (mg/dl)	219.58 ± 48.98	210.74 ± 29.80	p>0.05
HDL-cholesterol (mg/dl)	48.95 ± 10.36	50.16 ± 9.78	p>0.05
LDL-cholesterol (mg/dl)	130.58 ± 36.10	126.45 ± 24.78	p>0.05
TG (mg/dl)	173.16 ± 73.82	172.54 ± 68.83	p>0.05

BMI = Body Mass Index, WHR = Waist / Hip Ratio, SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure, AST = Aspartate aminotransferase ALT= Alanine aminotransferase, T. Cholesterol = Total cholesterol, HDL-cholesterol = High Density cholesterol, LDL-Cholesterol= Low Density Cholesterol, TG = Triglyceride

group during the treatment. Changes that occurred between pretreatment and after the 12-week treatment in body parameters and biochemical parameters of blood in sibutramine and placebo groups are presented in Tables 2 and 3.

Discussion

Many methods and treatments are used for the treatment of obesity. In order to be successful, these methods and treatments should be effective against etiologic mechanisms that lead to obesity. Thus, an ideal drug should decrease energy intake, prevent absorption of food, increase energy consumption, maintain the level of weight loss and have few side effects (7-9).

Sibutramine is a drug that blocks the reuptake of 5-HT and NA from nerve endings by its metabolites (6,7). The minimum effective dose of sibutramine with the least side effects is 10 mg/day (7). Hanotin (10) and Lean (11) showed in their studies that sibutramine exercised its optimal effect with daily doses of 10-15 mg. They found that at doses less than 10 mg sibutramine's effect on weight loss was lower and 5 mg/day dose was equivalent to placebo. No statistical difference between the doses more than 15 mg/day and 10-15 mg/day was found. Moreover, side effects of sibutramine were more prevalent at doses over 15 mg/day (7). In our study, we recommended our patients that sibutramine 10 mg/day (or placebo) be taken in the mornings before breakfast.

Success rate of diet alone or sibutramine alone on weight loss is low. Apfelbaum et al. (12) reported that low-calorie diet was effective in rapid weight loss and that this effect progressively decreased in the long-term. However, with the combination of low-calorie diet and sibutramine, weight loss was maintained for the duration of the therapy. According to Hansen et al. (13) administration of 10-15 mg/day sibutramine alone (without diet) for a long-term increases energy expenditure and is superior to placebo in weight loss. We have consulted a dietitian about the diet. Normal body weight of patients corresponding to their height was calculated and 24 calories/kg/day diet was administered in combination with sibutramine 10 mg/day (or placebo).

In their studies, Apfelbaum et al. (12) administered a very low-calorie diet + sibutramine 10 mg/day to 82 obese individuals and a very low-calorie diet + placebo to 78 obese individuals. Forty patients in sibutramine group (78%) and 18 patients in placebo group (40%) completed the study and these patients lost weight during the study. In comparison to the placebo group, body weight decreased significantly in sibutramine group ($p<0.05$). At the end of three months sibutramine group and placebo group rapidly lost weight, but in the subsequent months placebo group stopped losing weight and even an increase in weight was observed. Although rate of weight loss decreased in the sibutramine group after the first 3 months, it was maintained for the whole year.

Lean et al. (11) found that after one-year therapy placebo group lost 1.8 kg, sibutramine 10 mg/day group lost 4.8 kg and sibutramine 15 mg/day group lost 6.1 kg on average. Association between weight loss with sibutramine 10 mg/day and 15 mg/day was not significant, but association between weight loss with sibutramine 10 mg/day or 15 mg/day and that of placebo was found to be significant.

Hanotin et al. (10) found that after one-year therapy placebo group lost 1.4 kg, sibutramine 5 mg/day group lost 2.4 kg, sibutramine 10 mg/day group lost 5.1 kg and sibutramine 15 mg/day group lost 4.9 kg on average. They showed that 10 mg/day and 15 mg/day sibutramine doses had equivalent effects on weight loss, but were more effective than 5 mg/day sibutramine and placebo.

In our study we have divided our patients into two groups. Patients in the first group received diet + sibutramine 10 mg/day for 12 weeks and the other group received diet + placebo for 12 weeks. Sibutramine group lost 9.30 kg and diet + placebo group lost 5.27 kg on average. A statistically significant difference was found between pretreatment and post-treatment weight in the two groups ($p<0.05$ for each of them), but when sibutramine and placebo groups were compared with respect to weight loss, a difference of 4,03 kg was found; this difference was not considered to be statistically significant. Our results on weight loss were consistent with the results of Lean (11), Hanotin (10) and Fanghanel (14).

Fanghanel et al. (14) showed that BMI decreased 3.14 kg/m^2 in the sibutramine group and 1.46 kg/m^2 in the placebo group. The difference between two groups was considered statistically significant ($p<0.05$). In our study BMI decreased 4.10 kg/m^2 on average compared to baseline ($p<0.05$) in the sibutramine group and 2.26 kg/m^2 on average compared to baseline ($p<0.05$) in the placebo group. The difference between BMIs of sibutramine and placebo groups after the 12-week therapy was not considered statistically significant.

Gaal et al. (15) observed that waist/hip ratio and abdominal/visceral fat ratio were significantly lower in patients who received sibutramine 15 mg/day for six months, compared to those who received placebo. Lean et al (11) observed that waist/hip ratio was significantly lower in obese individuals who received sibutramine 15 mg/day for 12 months than in those who were given placebo and this decrease was statistically significant. Fanghanel et al (14) found that waist/hip ratio decreased 0.03 on average in patients who received sibutramine 10 mg/day plus placebo for six months and there was no significant difference between two groups. In our study waist/hip ratio decreased 0.02 in the sibutramine group and 0.01 in the placebo group. Although the decrease observed in sibutramine group was more than that in placebo group, the difference between the two groups was not statistically significant. Our WHR results were inconsistent with those reported by Gaal (15) and Lean (16), but consistent with those of Fanghanel et al. (14).

Improvement in serum lipid parameters was consistent with the amount of weight loss (7). Apfelbaum et al. (12) found that triglyceride level decreased and HDL-cholesterol and LDL-cholesterol levels increased in obese individuals who were given very low-calorie diet and sibutramine. In two separate studies performed by Lean et al. (11, 16) it was demonstrated that serum triglyceride level and LDL-cholesterol level decreased and HDL-cholesterol increased with sibutramine in obese and dyslipidemic patients. In a study by Rissanen (17), blood glucose regulation became steadier, triglyceride level and LDL-cholesterol level decreased and HDL-cholesterol level increased when sibutramine 15 mg/day was administered to Type 2 diabetic obese patients for 1 year. Fanghanel et al. (14) reported that total cholesterol, triglyceride and LDL-cholesterol levels decreased and HDL-cholesterol level increased in obese patients with 10 mg/day sibutramine. Yılmaz et al. (18) observed that total cholesterol and HDL-cholesterol levels decreased and HDL-cholesterol level increased in obese patients on sibutramine 10 mg/day for 1 year. At the end of our 3 month study, triglyceride level ($p<0.05$), total cholesterol level ($p<0.05$) and LDL-cholesterol level ($p<0.05$) decreased and HDL-cholesterol level increased ($p<0.05$) in the sibutramine group. No significant change was observed in triglyceride, total cholesterol, LDL-cholesterol and HDL-cholesterol levels in our obese patients who were given placebo. These results are consistent with those reported in the literature.

Sibutramine has no direct effect on blood glucose. However weight loss with sibutramine may help blood glucose control in obese type 2 diabetic patients (7,19). In our study 13 patients were found to have impaired OGTT (9 patients in sibutramine group and 4 patients in placebo group). After 12-week therapy OGTT impairment was still observed in 7 patients (5 patients in sibutramine group and 2 patients in placebo group) and 6 patients (4 patients in sibutramine group and 2 patients in placebo group) had improved OGTT. This suggests that OGTT impairment could be improved by weight loss in half of our obese patients with this impairment.

Cardiovascular side effects of sibutramine are consistent with its mechanism of action as a 5-HT and NA reuptake inhibitor (SNRI). Such side effects are observed also with other SNRIs. These drug-related side effects decrease upon discontinuation of the drug (7).

Apfelbaum et al. (12) found that blood pressure increased 1.5 mm Hg on average in patients who received low-calorie diet in combination with sibutramine and decreased 1.9 mm Hg in patients who received placebo. In addition, pulse rate increased 8 beat per minute on average in sibutramine group and 1 bpm on average in placebo patients. ECG examinations revealed no pathologic findings. In a study by Hanotin et al. (10) there was no significant difference in 10 mg/day sibutramine group in systolic and diastolic blood pressures. However, heart rate increased 5 bpm on average. No difference was found in ECG. Fanghanel et al. (14) observed an

increase in both systolic and diastolic blood pressures in obese patients who received sibutramine 10 mg/day for 6 months and a decrease in systolic and diastolic blood pressures in the placebo group. No change was observed in pulse rate and no pathologic findings were observed in ECG examinations. Lean (11) observed that therapy with sibutramine 10 mg/day decreased both systolic and diastolic blood pressures by 2 mm Hg on average in normotensive obese individuals. In hypertensive obese patients, diastolic blood pressure decreased by 5.9 mm Hg on average with 10 mg/day sibutramine and placebo administration reduced systolic blood pressure by 4 mm Hg on average. Twenty four weeks after the therapy, obese patients who lost weight experienced a 7 mm Hg decrease in blood pressure. In addition, it was found that sibutramine 10 mg/day increased pulse rate by 4 beats per minute.

In our study, 10 mg/day sibutramine group experienced an increase of 2.9 mm Hg on average in systolic blood pressure and an increase of 0.4 mm Hg on average in diastolic blood pressure after the treatment. Placebo group experienced a mean increase of 1.66 mm Hg in systolic blood pressure and a mean increase of 0,37 mm Hg in diastolic blood pressure. The difference between the two groups in terms of the increase in systolic and diastolic blood pressures was not considered statistically significant. Our patients on sibutramine therapy experienced an increase of 4 beats per minute on average and placebo patients experienced an increase of 2 beats per minute on average. When the increase in heart rate in sibutramine group after treatment was compared with that in the placebo group, it was considered statistically significant ($p<0.05$). We did not observe any pathologic findings suggesting rhythm disorder and ischemic heart disease in ECG follow-ups. Cardiovascular side effects of sibutramine that we observed in our study were consistent with those reported in literature.

Heal et al. (6) suggested that d-phenfluramine and mazindol, which exercise their effects by monoamine release, may lead to pulmonary hypertension. But, sibutramine inhibits monoamine reuptake, so it does not cause pulmonary hypertension. Bach et al. (20) reported that in their 7-month study with 133 sibutramine patients and 77 placebo patients, prevalence of valvular heart disease was equal in both groups. Thus, the potential of sibutramine to result in new valvular heart disease was found to be equal to placebo. In our study we have performed echocardiographic examination in our patients both before and after the treatment. We did not observe findings of recently developed valvular heart disease or pulmonary hypertension during therapy in our sibutramine and placebo groups. Our results are consistent with those reported by Heal (6) and Bach (20).

Side effects related to sibutramine use for treatment of obesity: the most frequently reported side effects in the studies of Apfelbaum (12), Hanotin (10) and Lean (7) were constipation, pharyngitis, dry mouth, headache, insomnia, dizziness, palpitations and flushing. Discontinuations due to these side effects were not common. In a study by Apfelbaum et al. (12), 2 out of 82 patients in sibutramine group and 5 out of 78 patients in placebo group discontinued the treatment. In a study by Hanotin et al. (28) 4 out of 59 patients in the placebo group, 4 out of 59 patients in sibutramine 10 mg/day group and 5 out of 62 patients in sibutramine 15 mg/day group discontinued treatment. In the above-mentioned studies, reasons for discontinuation included hypertension, headache, insomnia and pregnancy. In our study, side effects observed in obese patients who received sibutramine 10 mg/day and placebo were similar to those reported by Apfelbaum (12), Hanotin (10) and Lean (11). No severe side effect leading to discontinuation was observed. Two patients in sibutramine group discontinued treatment. One of these patients discontinued treatment due to having more difficulty in controlling the existing hypertension and the other for umbilical hernia. Only one patient in the placebo group discontinued treatment for severe depression that developed during treatment.

In conclusion, we observed that low-calorie diet and sibutramine 10 mg/day use were more effective than placebo in weight loss. However when we compared the amount of weight loss we could not observe any significant difference. Moreover, we concluded that sibutramine affected lipid parameters favorably, was not associated with very important complications leading to discontinuation and did not have any negative effect on heart valves.

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