Cardiac valve evaluation and adipokine levels in obese women treated with sibutramine

Sibutramin ile tedavi edilen obez kadınlarda kardiyak kapak değerlendirmesi ve adipokin düzeyleri

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Abstract

Objective: The aims of present study were 1) to evaluate cardiac valve characteristics, 2) to determine the plasma concentrations of fibrinogen, high sensitivity C-reactive protein (hsCRP), adiponectin, and tumor necrosis factor-α (TNF-α) in the obese women before and after 19 months sibutramine treatment in the obese women.

Methods: Sixty obese women were enrolled in this prospective, randomized study. Thirty women received 10 mg once daily dose of sibutramine for 19 months. The rest of the obese women received 15 mg once daily dose of sibutramine for 19 months. All patients were evaluated with echocardiography. Plasma levels of adiponectin and TNF-α were measured by enzyme-linked immunosorbent assay (ELISA) and hsCRP by immunoturbimetric assay. Student paired and unpaired t tests were used to compare the 10 mg or 15 mg dose sibutramine effects either in groups or between the groups.

Results: There were no signs of significant regurgitation or thickening of the mitral and aortic valves on echocardiographic evaluation performed after 19 months of treatment. Parameters of systolic function after 10 or 15 mg treatment were not different from pretreatment characteristics. Minimal tricuspid regurgitation was found in one (1/27) patient treated with 10 mg sibutramine after 19 months. Among obese patients treated with 15 mg sibutramine one patient (1/28) had minimal mitral valve regurgitation and 2 patients (2/28) had minimal aortic insufficiency. Stage II diastolic dysfunction in the 15 obese treated with 15 mg regressed to stage I diastolic dysfunction (50%). Stage II diastolic dysfunction in the 10 obese treated with 10 mg regressed to stage I diastolic dysfunction (33.3%). Mean levels of TNF-α(p=0.04), fibrinogen (p=0.03) and hsCRP (p=0.04)i decreased and adiponectin (p=0.03) levels increased in the obese treated with 10 mg sibutramine. Likewise, in the patients treated with 15 mg sibutramine, mean levels of TNF-α(p=0.01), fibrinogen (p= 0.02), and hsCRP (p= 0.04) decreased and adiponectin (p= 0.02) levels increased.

Conclusion: Nineteen months of sibutramine treatment does not affect heart valve and systolic functions, however, diastolic dysfunction severity reduced with sibutramine treatment. Also In addition, mean levels of adiponectin, TNF- α, fibrinogen and hs- CRP change with 19 months sibutramine treatment. *(Anadolu Kardiyol Derg 2010; 10: 226-32)*

Key words: Sibutramine, echocardiography, cardiac valve, adipokine, obesity

Özet

Amaç: Bu çalışmada; ilk olarak 19 ay süreyle 10 mg veya 15 mg sibutramin kullanımıyla kapak fonksiyonlarının değerlendirilmesi, ikinci olarak ta sibutramin tedavisi öncesi ve sonrasında fibrinojen, yüksek duyarlı C-reaktif protein (hsCRP), adiponektin ve tümör nekroz faktör-α (TNF-α) plazma düzeylerinin karşılaştırılması amaçlandı.

Yöntemler: Bu prospektif randomize çalışmaya 60 obez kadın alındı. Otuz obez kadına, 10 mg sibutramin ve diğer 30 kadına 15 mg sibutramin 19 ay süreyle verildi. Tüm hastalar tedavi öncesi ve sonrasında Doppler ekokardiyografi ile değerlendirildi. Adiponektin ve TNF-α düzeyleri; enzyme-linked immunosorbent issay (ELISA) yöntemiyle ölçüldü. İmmunoturbimetrik yöntemle hsCRP düzeyi saptandı. On veya 15 mg dozunda sibutramin etkilerini, hem grup içi hem de gruplar arası değerlendirmek amacıyla eşleştirilmiş ve eşleştirilmemiş Student t testleri kullanıldı.

Bulgular: Tüm olgular 19 ay sonrasında değerlendirildiğinde; regürjitasyon, aort veya mitral kapakta kalınlaşma saptanmadı. Ondokuz ay 10 mg sibutramin kullanan grupta, minimal triküspid regürjitasyonu 1 (1/27) hastada saptandı. Ondokuz ay süreyle 15 mg sibutramin kullanan grupta, minimal mitral kapak regürjitasyonu 1 (1/28) ve minimal aort yetmezliği 2 (2/28) hastada saptandı. Evre II diyastolik disfonksiyon, 15 mg sibutramin tedavisiyle evre I diyastolik disfonksiyona 15 (%50) hastada geriledi. Bu oran 10 mg sibutramin tedavisiyle daha düşük düzeydeydi (10/30) (%33.3).

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Ortalama TNF-α (p=0.04), fibrinojen (p=0.03) ve hsCRP (p=0.04) düzeyleri, 10 mg sibutramin tedavisiyle azalırken, adiponektin (p=0.03) seviyelerinde artış saptandı. Benzer olarak, 15 mg sibutramin tedavisiyle, TNF-α (p=0.01), fibrinojen (p=0.02) ve hsCRP (p=0.04) düzeylerinde azalma sağlanırken, adiponektin (p=0.02) seviyelerinde artış saptandı.
Sonuç: Ondokuz ay sibutramin tedavisiyle kapak fonksiyonları etkilenmez, ancak diyastolik disfonksiyon şiddetinde azalma saptandı. Ayrıca, adiponektin, TNF-α, fibrinojen ve hsCRP düzeyleri 19 ay sibutramin tedavisiyle değişir. *(Anadolu Kardiyol Derg 2010; 10: 226-32)*
Anahtar kelimeler: Sibutramin, ekokardiyografi, kardiyak kapak, adipokin, obezite

Introduction

Obesity has become increasingly prevalent worldwide over the recent years and it is expected that the problem of overweight will extend in future. Obesity is associated with increased morbidity and mortality (1-3, 5-8, 13). Pharmacological agents are often useful adjuncts to dietary therapy in causing weight loss. The prolonged use of adrenergic or serotoninergic anorectic drugs induce several adverse effects (4, 12). Previously, severe heart valve disorders have been reported in patients receiving a combination of the anorectic drugs such as fenfluramine and phentermine (8, 9). Likewise, some studies indicated that use of dexfenfluramine and phentermine/fenfluramine was associated with an increase in the prevalence of aortic regurgitation, but was not associated with an increase in the prevalence of mitral regurgitation (9, 10). The serotonin-releasing agents have been implicated as a cause of acquired aortic and mitral valve abnormalities (11).

However, sibutramine differs from drugs such as fenfluramine and d-fenfluramine (12-14). Bach et al. (12) suggested that sibutramine did not appear to cause cardiac valve disease, because, it does not influence serotonin release.

Obese subjects typically are in proinflammatory state that may predispose them to acute cardiovascular morbidity and mortality (16-18). Elevated circulating levels of cytokines and inflammatory markers, such as interleukin- 6 (IL- 6), C-reactive protein (hsCRP) and tumor necrosis factor-alpha (TNF-α) have been implicated to play role in the obesity (16, 19, 21, 22). Previous studies demonstrated that sustained weight loss was associated with reduction of cytokines (23, 24) and improved insulin sensitivity (15, 28). Marfella et al. (25) suggested that mean levels of TNF-α and hsCRP were decreased in obese women that lost at least 10% of their original weight, after 1 year of a multidisciplinary program of weight reduction. In addition, many studies showed that adiponectin levels changed with weight loss (26, 27). However, in a recent study, treatment with sibutramine 15 mg once daily effectively reduced weight and enhanced insulin sensitivity without alteration of serum adiponectin levels in obese patients with type 2 diabetes (28).

The aims of present study were 1) to evaluate cardiac valve characteristics, 2) to determine the plasma concentrations of fibrinogen, hsCRP, adiponectin, and TNF-α in the obese women before and after 19 months of sibutramine treatment.

Methods

Study design

Nineteen months, prospective, randomized trial was designed to evaluate the effects of a treatment with sibutramine on echocardiographic parameters, hsCRP, adiponectin and TNF-α levels. Sixty obese women were enrolled in the study. Thirty obese women (mean age 39.6±2.0 years) received 10 mg once daily dose of sibutramine for 19 months. The rest of the obese (mean age 40.6±8.1 years) women received 15 mg once daily dose of sibutramine for 19 months. The local Ethics committee approved the protocol study and all subjects gave informed consent. The study was performed between March 2004 and March 2007.

Inclusion criteria were age 20-60 years and body mass index (BMI) 25-40 kg/m^2. Exclusion criteria were systolic blood pressure greater than 140 mmHg; diastolic blood pressure greater than 85 mmHg, obesity of endocrine origin, type 1 diabetes mellitus or type 2 diabetes mellitus treated with insulin or poorly controlled (fasting glycemia, >7.8 mmol/L or 1.40 g/L), significant cardiac dysfunction, life-threatening systemic disease, significant pulmonary disease, and presence of any other significant medical illness. Pregnancy was also categorized as exclusion criteria.

The program included the taking of full medical history and physical examinations, urinalysis, blood chemistry, echocardiography. The physical examination and biochemical tests were performed by same doctor at each three months. Each patient underwent transthoracic two-dimensional echocardiography prior to the treatment and at the end of the study. Blood pressure, heart rate, weight, height, BMI and waist-to-hip ratio (WHR) were measured.

Echocardiographic examination

Transthoracic echocardiographic examinations were conducted with the subjects in the left lateral position. All echocardiograms were performed by the same experienced cardiologist. Transthoracic echocardiography was performed using current generation two-dimensional echocardiographic scanners (Vivid 3, General Electric, 3.5-MHz transducer, Milwaukee, USA). Evaluation of valve disease was performed using the semiquantitative and quantitative methods recommended by the American Society of Echocardiography (29). The determination of the planimetric valves area (mitral valve area, MVA) for stenosis, evaluation of annulus diameter for regurgitation and detection of diastolic and systolic function anomalies based on valve flow velocity patterns for mitral, tricuspid, aortic and pulmonary valves were evaluated by 2-dimensional and pulsed Doppler echocardiography. Structural alteration in the cusps and annulus of the aortic and mitral valves were diagnosed by thickened and bright echoes. Significant aortic stenosis was defined as cusps separation of less than 15 mm and a maximum aortic flow velocity greater than 2.2 m/s. Significant regurgitation was

defined as a regurgitation jet on the color and pulsed Doppler echocardiograms extending more than 2 cm behind the plane of the aortic, mitral or tricuspid valve and pandiastolic (aortic regurgitation) or pansystolic (mitral and tricuspid regurgitation) regurgitant flow of more than 2 m/s on continuous wave Doppler (29, 30). The severity of valvular regurgitation was determined on a qualitative scale according to the American Society of Echocardiography guideline for the management of patients with valvular heart disease: mild (grade 1), moderate (grade 2) and severe (grade 3-4) (29).

Left ventricular (LV) dimensions were measured from M-mode images acquired from the parasternal long-axis view: interventricular septum thickness (IVST), posterior wall thickness (PWT), LV end-diastolic diameter (LVEDD), LV end- systolic diameter (LVESD), fractional shortening (FS) and LV ejection fraction (LVEF).

Three stages of diastolic dysfunction were recognized (31). Stage I was characterized by reduced left ventricular filling in early diastole with normal left ventricular and left atrial pressures and normal compliance. Stage II or pseudonormalization was characterized by a normal Doppler echocardiographic transmitral flow pattern because of an opposing increase in left atrial pressures. This normalization pattern was a concern because marked diastolic dysfunction can easily be missed. Stage III was characterized by severe restrictive diastolic filling with a marked decrease in left ventricular compliance.

Biochemistry laboratory tests

Serum concentrations of glucose, triglyceride, total and high-density lipoprotein (HDL)-cholesterol were determined by enzymatic procedures, serum insulin was measured by chemiluminescence's test, hsCRP - by immunoturbimetric assay and fibrinogen - by coagulation method. Plasma levels of adiponectin and TNF-α were measured by enzyme-linked immunosorbent assay (ELISA). The intra-assay and inter-assay coefficients of variation (CVs) were as following: adiponectin (BIOSOURCE, ELISA, Belgium) - 4.2 and 4.7%, TNF-α (DIACLONE, Human TNF-α ELISA, France) - 3.3 and 9%.

Insulin resistance was estimated using the homeostasis model assessment (HOMA) from fasting glucose and insulin concentrations using the following formula (32).

$$\text{HOMA-IR} = \frac{(\text{fasting plasma insulin}[\mu U/ml]) \times (\text{fasting plasma glucose}[mmol/l])}{22.5}$$

Statistical analysis

Data were analyzed with SPSS version 13.0 software (SPSS, Chicago, IL, USA). Values are expressed as mean±SD. Student paired and unpaired t tests were used to evaluate the 10 mg or 15 mg dose sibutramine effects within and between the 2 groups.

Results

Three obese treated with 15 mg sibutramine and 2 obese treated with 10 mg sibutramine were lost during follow-up. Nobody of the rest participants of the study discontinued the drug therapy due to adverse effects. The most common reported adverse effects were dry mouth (9 patients), headache (4 patients) and constipation (8 patients) in group treated with 10 mg sibutramine. After 2 weeks of treatment, nobody complained of dry mouth and headache. In obese treated with 15 mg, adverse effects were dry mouth (14 patients), headache (9 patients) and constipation (12 patients). At the end of 4th week, nobody complained of dry mouth.

Demographic and laboratory characteristics of patients are summarized in Table 1. Mean levels of BMI in the obese treated with 10 mg significantly decreased after 19 months (p=0.01). Similarly, mean levels of BMI in the obese treated 15 mg decreased at the end of study (p=0.003). After the treatment, all patients lost a significant amount of weight compared to the baseline values: 10 mg sibutramine group - 13.2%, (p= 0.001), and 15 mg sibutramine group - 13.0% (p= 0.03). Average systolic and diastolic blood pressures of patients treated with 10 mg or 15 mg sibutramine increased after treatment, but not statistically significant.

In both of groups, HOMA-IR levels did not change with sibutramine 10 and 15 mg. Mean levels of adiponectin increased (by 6%, p=0.03), while mean levels of TNF-α (by -16%, p=0.04), fibrinogen (by -5%, p=0.03) and hsCRP (by -16.6% p=0.04) reduced markedly in obese treated with 10 mg of sibutramine. Similarly, mean levels of adiponectin increased by 16.6% (p=0.002), TNF-α decreased by 29.4% (p=0.001), fibrinogen level reduced by 10.2% (p=0.002) and hsCRP decreased by 12.5% (p=0.05) in the patients treated with 15 mg of sibutramine for 19 months.

Positive changes in lipid parameters were observed following sibutramine, particularly 15 mg therapy. Mean levels of total cholesterol (p=0.001), low-density lipoprotein cholesterol (p=0.01) and triglyceride (p=0.001) levels decreased significantly and mean HDL-cholesterol levels increased (p=0.05) as compared with the baseline values in obese treated with 15 mg sibutramine.

Echocardiographic variables are shown in Tables 2 and 3. Regurgitation or thickenings of the mitral and aortic valves were not determined prior to the medication use. Mild tricuspid regurgitation was found in one (1/27) patient treated with 10 mg sibutramine after 19 months of treatment. In obese treated with 15 mg, single (1/28) mild mitral valve regurgitation and 2 (2/28) mild aortic insufficiency were seen. Stage II diastolic dysfunction regressed to stage I in 15 of 30 (50%) obese treated with 15 mg and in 10 of 30 (33.3%) obese treated with 10 mg. Systolic functions in the patients treated with 10 mg and 15 mg did not change after treatment (p=0.09, p=0.90). At the beginning of the drug, mean levels of left ventricular thickness in the obese treated with 10mg and 15 mg sibutramine were found to be 0.9±0.01 mm and 0.79±0.02 mm (p=0.09), respectively. After treatment, mean levels of left ventricular thickness in patients treated 10mg and 15 mg were found to be 0.88±0.05 mm and 0.90±0.01 mm (p= 0.85), respectively.

Discussion

This study demonstrates that 19 months of treatment with 10 mg or 15 mg sibutramine are not associated with increased

Table 1. Patient's characteristics before and after 19 months of sibutramine treatment

Variables	Sibutramine 10 mg (n=30)			Sibutramine 15 mg (n=30)		
	Before	After	p	Before	After	p
Age, years	39.6±2.1			40.6± 8.1		
Body weight, kg	93.1±9.6	80.8±7.7	0.001	95.1±10.9	82.7±4.7	0.03
Body mass index, kg/m^2	31.5±2.0	27.4±2.9	0.01	30.9±4.8	26.5±4.1	0.003
Waist circumference, cm	109.7±14.0	96.7±7.2	0.04	117.5±19.6	106.6±17.0	0.02
SBP, mmHg	122.3±8.5	124.0±10.2	0.12	125.5±8.0	129±12.8	0.08
DBP, mmHg	59.3±6.8	62.0±5.7	0.42	55.1±10.1	59.9±5.7	0.8
Heart rate, pulse/min	75.5±10.5	77.6±9.1	0.98	78.6±11.3	80.1±11.1	0.97
Triglyceride, mg/dl	124.2±39.8	120.1±41.8	0.09	145.8±27.0	121.8±39.8	0.001
Total-Cholesterol, mg/dl	243.0±42.9	240.7±40.6	0.95	251.9±30.0	200.1±44.2	0.001
LDL-Cholesterol, mg/dl	123.0±28.7	121.5±30.1	0.09	133.0±28.7	120.3±32.9	0.01
HDL-Cholesterol, mg/dl	43.3±11.2	43.0±17.7	0.89	45.5±11.2	50.3±9.2	0.05
Fasting glucose, mg/dl	96.9±6.2	93.8±5.3	0.07	95.05±5.87	89.4±11.7	0.05
Fasting insulin, µU/L	9.0±0.7	6.5±1.6	0.02	11.6±3.2	8.4±2.2	0.03
HOMA-IR	1.7±0.1	1.9±0.8	0.07	2.3±0.3	2.0±0.8	0.09
Fibrinogen, mg/dl	401.5±35.3	379.1±38.2	0.03	445.8±41.9	400.0±60.7	0.002
HsCRP, mg/dl	0.30±0.1	0.25±0.8	0.04	0.32±0.6	0.28±0.1	0.05
Adiponectin,µgr/ml	5.6±1.1	6.0±1.2	0.03	5.4±1.9	6.3±0.7	0.002
TNF-α ,pg/ml	3.0±1.1	2.5±10.9	0.04	3.4±1.5	2.4±0.7	0.001

Data are expressed as mean±SD
Student's t test for paired samples
DBP - diastolic blood pressure, HDL - high-density lipoprotein, HOMA-IR- homeostasis model assessment-insulin resistance, hsCRP - high sensitivity C reactive protein, LDL - low-density lipoprotein, SBP - systolic blood pressure, TNF-α - tumor necrosis factor-α

Table 2. Doppler echocardiography-derived cardiac valve area before and after 19 months of treatment with sibutramine

Valve area (normal values), cm^2	Sibutramine 10 mg (n=30)			Sibutramine 15 mg (n=30)		
	Before	After	p	Before	After	p
Aortic valve (2.6-3.5)	2.91±0.26	2.83±0.78	0.90	2.99± 0.98	3.09± 0.71	0.90
Mitral valve (4.0-6.0)	5.15±0.99	5.02±0.35	0.10	4.90±0.17	5.07±0.32	0.75
Tricuspid valve (7-10)	10.4±1.07	10.89±1.01	0.75	10.61±0.65	10.54± 0.99	0.85
Pulmonary valve (6-8)	7.90±0.09	7.89±0.98	0.76	7.50±0.97	7.65± 1.09	0.90

Data are expressed as mean±SD
Student's t test for paired samples

Table 3. Planimetric cardiac valve area before and after 19 months of treatment with sibutramine

Normal valve area (normal values), cm^2	Sibutramine 10 mg (n=30)			Sibutramine 15 mg (n=30)		
	Before	After	p	Before	After	p
Aortic valve (2.6-3.5)	2.80±0.11	2.91±0.71	0.75	3.01±0.18	2.99±0.67	0.85
Mitral valve (4.0-6.0)	5.76±0.75	5.45±0.35	0.90	4.85±0.89	5.00±0.12	0.15
Tricuspid valve (7-10)	9.98±1.11	10.00±1.65	0.09	10.00±1.11	9.84±0.77	0.77
Pulmonary valve (6-8)	7.75±0.12	7.81±1.00	0.88	7.51±0.97	7.62±1.35	0.95

Data are expressed as mean±SD
Student's t test for paired samples

prevalence of valvular heart disease. In addition, our findings suggested that diastolic dysfunction improved with sibutramine treatment, particularly. However, no change in the systolic function with sibutramine treatment was seen. In addition, mean levels of TNF-α, hsCRP and adiponectin changed markedly with sibutramine.

Previously, some larger studies have confirmed an excess prevalence of mitral and aortic valve pathology among patients exposed to fenfluramine, either with or without phentermine (9, 33-37). The mechanism of acquired left-sided valve abnormalities associated with fenfluramine and dexfenfluramine has not been determined, but both fenfluramine and dexfenfluramine are serotonin-releasing agents. The pharmacologic action of fenfluramine-containing products is theorized to be the cause of the pulmonary and valvular problems. Not only do fenfluramine and dexfenfluramine inhibit the reuptake of serotonin in the central nervous system (CNS), but their active metabolite, norfenfluramine, increases the release of serotonin by activating serotonin receptors (13). The valvular abnormalities that have been seen are morphologically similar to those noted in patients with the carcinoid syndrome (20, 32). Bach et al. (12) found that the prevalence of left- sided cardiac valve dysfunction was not higher than background in obese patients treated with sibutramine for an average of 7.6 months. The prevalence of left-sided cardiac valve dysfunction was low and similar for the two treatment groups (sibutramine 3/133, or 2.3%; placebo 2/77, or 2.6%). Similarly, de Simone et al. (38) reported that 15 mg sibutramine treatment was not associated with onset or increased severity of valve regurgitation, after 3 months of therapy. In the present study, mitral or aortic valves regurgitation was observed in none of patients treated 10 mg sibutramine. Minimal mitral valve regurgitation was seen in one patient treated with 15 mg sibutramine and minimal aortic insufficiency was seen in two patients treated with 15 mg sibutramine. This study suggested that 19 months treatment of sibutramine was not associated with severe valve disease. Previously studies reported the frequency of valvular dysfunction in patients taking appetite suppressants varied between 6 and 25% (10, 11). This wide variation was explained by the different research methods used, different drug doses and variable duration of therapy (39). In the present study, frequencies of minimal valvular disease were 3.7% and 10.7% in patients treated with 10 mg and patients treated with 15 mg sibutramine, respectively.

Sibutramine, a serotonin and noradrenaline reuptake inhibitor, has been shown to be an affective agent for weight loss and maintenance. According with its known pharmacology, sibutramine increased blood pressure by 1 to 3 mmHg and pulse rate by 4 to 5 beats per minute; however, the overwhelming majority of obese patients did not have significant hemodynamic changes with sibutramine treatment (41). In a recent study, adverse events related to high blood pressure and/or pulse rate were reported in less than 0.2% of patients (40). Similarly, we did not find any differences in blood pressures and pulse rates before and after treatment (10 mg or 15 mg).

It is known that obesity may be complicated with impaired systolic and diastolic functions (1). Previously, Godoy-Matos et al. (42) reported that echocardiographic parameters of diastolic dysfunction in patients treated with sibutramine did not change significantly. However, in the present study, echocardiographic parameters of diastolic dysfunction changed with 10 and 15 mg sibutramine treatment in the obese patients, but not systolic function.

In recent years, several studies have demonstrated changes in plasma adipocytokines concentrations in response to weight loss (23-26). It has been shown consistently that insulin resistance, leptin and TNF-α levels decreased (17, 43) and adiponectin increased (27) with weight reduction. Also, levels of CRP, a low grade inflammatory marker, fall with weight reduction obtained by a non-pharmaceutical approach (44). In a recent study, no change in CRP level was reported following a weight reduction of 2.5% with orlistat, but CRP did fall following a 5.4% weight reduction in the sibutramine-treated subjects (45). Modest weight loss with sibutramine treatment could be achieved to produce a decrease in CRP levels. However, Abbasi et al. (46) showed that there were no alteration in serum adiponectin concentrations with significant improvement in insulin resistance after sibutramine treatment in insulin-resistant obese non-diabetic patients. Likewise, Hung et al. (28) demonstrated that sibutramine treatment effectively reduced weight and enhanced insulin sensitivity without an alteration in serum adiponectin concentrations in obese type 2 diabetic patients. In other study, Tambascia et al. (15) suggested that 6 months sibutramine treatment was effective in improving of HOMA-IR with no change in fibrinogen levels in the non-diabetic women. In the present study, mean levels of HOMA-IR in the obese did not change with 10 mg and 15 mg sibutramine treatment. However, mean levels of adiponectin increased while mean levels of hsCRP and TNF-α decreased with sibutramine. These findings suggest that the impact of weight reduction with 19 months sibutramine treatment is more profound on adiponectin, fibrinogen, hsCRP, and TNF-α levels than on HOMA-IR.

Study limitations

Our study assessed the effects of 19 months treatment with sibutramine 10 mg or 15 mg on cardiac valve characteristics and left ventricular functions. However, we did not evaluate the effects of the drug in long-term use. It is known that serotonin metabolism seems to be a likely mechanism for development of the drug-induced valvular heart disease. However, we did not investigate the relationship between serotonin metabolism and valvular characteristics, as well as the relationships between adipocytokines and valvular characteristics.

Conclusion

Nineteen months of sibutramine treatment (10 mg or 15 mg) does not affect heart valve morphology and systolic functions, however, diastolic function improves with sibutramine treatment. In addition, mean levels of adiponectin, TNF-α, fibrinogen and hsCRP change with 19 months of sibutramine treatment.

Conflict of interest: None declared.

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