Effect of weight loss on QTc dispersion in obese subjects

Obez bireylerde kilo kaybının QTc dispersiyonu üzerine etkisi

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ABSTRACT

Objective: Increased QTc dispersion is a predictor for ventricular arrhythmias. The aim of this study was to investigate whether QTc dispersion decreases after weight loss program with diet and medical treatment.

Methods: Total 30 (24 women and 6 men, mean age: 44±8 years) obese subjects who lost at least 10% of their original weight after 12 week weight loss program were included in present study. Obesity was defined as ≥30 kg/m2 of body mass index (BMI). Normal weight was defined as ≤ 25 kg/m2 of BMI.

Results: After 12 week weight loss program, BMI decreased from 42±5 kg/m2 to 36±4 kg/m2 (p<0.001) and mean weight of obese subjects decreased from 110±17 kg to 95±15 kg (p<0.001). The mean amount of weight loss was 14.5±5.0 kg (range 9-32 kg). The average percent of weight loss was 13% (10.0%-20.3%). Maximum QTc interval (from 446±19 ms to 433±27 ms, p=0.024) and QTc dispersion (from 66±18 ms to 52±25 ms, p=0.024) significantly decreased after weight loss program. A statistically significant correlation was found between decrease in level of QTc dispersion and amount of weight loss (r=0.487, p=0.007).

Conclusion: Substantial weight loss in obese subjects is accompanied by significantly decreased QTc dispersion. The degree of QTc dispersion reduction is associated with amount of weight loss. *(Anadolu Kardiyol Derg 2006; 6: 126-9)*

Key words: Obesity, weight loss, electrocardiographic marker, QTc dispersion

ÖZET

Amaç: Artmış QTc dispersiyonu ventriküler aritmiler için bir göstergedir. Bu çalışmanın amacı diyet ve medikal tedavi ile kilo kaybı programı sonrası QTc dispersiyonunun azalmasını araştırmaktır.

Yöntemler: Bu çalışmaya 12 haftalık kilo kaybı programı sonrası mevcut kilolarının en az %10'nu veren 30 (24 kadın ve 6 erkek, ort. yaş: 44±8 yıl) obez birey dahil edildi. Obezite vücut kitle indeksi'nin (VKİ) ≥30 kg/m2 olarak tarif edildi. Normal kilo ise VKİ'nin ≤ 25 kg/m2 olarak tarif edildi.

Bulgular: On iki haftalık kilo kaybı programı sonrası, VKİ 42±5 kg/m2'den 36±4 kg/m2 (p<0.001) azaldı ve obez bireylerin ortalama ağırlığı 110±17 kg'dan 95±15 kg (p<0.001) azaldı. Kilo kaybının ortalama miktarı 14.5±5.0 kg (9-32 kg arasında) idi. Kilo kaybının ortalama yüzdesi ise 13% (10.0%-20.3%) idi. Maksimum QTc interval (446±19 ms'den 433±27 ms, p=0.024) ve QTc dispersiyonu (66±18 ms'den 52±25 ms, p=0.024) kilo kaybı programı sonrası önemli oranda azaldı. QTc dispersiyonun seviyesindeki azalma ile kilo kaybının miktarı arasında istatistiksel olarak anlamlı ilişki bulundu (r=0.487, p=0.007).

Sonuç: Obez bireylerde önemli kilo kaybı QTc dispersiyon seviyesini önemli oranda azaltmıştır. QTc dispersiyon azalmasının derecesi kilo kaybının miktarı ile ilişkilidir. *(Anadolu Kardiyol Derg 2006; 6: 126-9)*

Anahtar kelimeler: Obezite, kilo kaybı, elektrokardiyografik marker, QTc dispersiyon

Introduction

Obesity, which is an important public health problem, is strongly linked to coronary mortality (1). Specifically, in severely obese men, a 6 to 12 fold excess of cardiovascular mortality rate was demonstrated (2) Ventricular tachyarrhythmias have been shown to be associated with obesity (2). Even, the occurrence of sudden death has been reported in obese patients without known heart abnormalities (3,4). Some electrocardiographic parameters may predict sudden deaths and ventricular arrhythmias. Dispersion of the QT interval, a measure of interleads QT variability, reflects regional variation in ventricular repolarization. An increased QT dispersion is thought to be a possible risk factor for ventricular arrhythmias and sudden death (5,6). Previous studies have been reported that morbid obesity is associated prolongation of QTc interval (7-9). Therefore, substantial weight loss in obese subjects may return to normal the increased QTc dispersion. Some studies have been reported that weight loss attained with different methods (diet and/or surgical) in obese subjects is accompanied with decrease of QTc interval prolongation (10,11).

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In the literature, information about decrease of QTc dispersion in obese subjects after weight loss with diet and medical treatment is also limited.

Therefore, the aim of this study was to investigate whether the decrease of QTc dispersion takes place after weight loss with diet and medical treatment.

Methods

Consecutive 37 obese subjects, admitted to cardiology and internal medicine outpatient clinics of our institute, were included in weight loss program. Medical history, physical examination, laboratory tests (complete blood count, electrolytes and thyroid hormones) and electrocardiographic (ECG) measurements were performed in all obese subjects of study population. All obese subjects were in sinus rhythm and none of them were taking any medications such as antiarrhythmic agents, tricyclic antidepressants, antihistaminics and antipsychotics. Subjects with thyroid dysfunction, anemia, electrolyte imbalance, known valvular heart disease, heart failure, and coronary artery disease, connective tissue disorders, left bundle branch block, and atrioventricular conduction abnormalities on ECG were excluded. After 12 week weight loss program, 7 obese subjects with weight loss lower than 10% of their original weight were excluded from the study. Totally, 30 (24 women and 6 men) obese subjects who lost at least 10% of their original weight were included in present study. Height and weight were directly measured using a standardized protocol. Body mass index (BMI) was calculated by dividing weight in kilograms by the square of the height in meters. Obesity was defined as ≥30 kg/m^2 of BMI. Normal weight was defined as ≤ 25 kg/m^2 of BMI.

Electrocardiography

All subjects underwent a routine standard 12-lead surface ECG recorded at a paper speed of 25 mm/s and gain of 10 mm/mV (Cardiofax V, Nihon Kohden Corp, Tokyo, Japan) in the supine position and were breathing freely but not allowed to speak during the ECG recording. To avoid diurnal variations, we generally took the ECG recordings of obese subjects at the same time (10.00-12.00 A.M.) before and after weight loss program. The ECG's were transferred to a personal computer via scanner and then were magnified by 400 times by Adobe Photoshop software. QT interval, which is the interval between beginning of QRS complex to the end of T wave, was measured in all derivations in which T wave was clearly seen and not mixed with an U wave. In all subjects, derivations in which the beginning and endpoint of QT interval could not be distinguished were excluded. The average of QT intervals measured in all of derivations was accepted as mean QT interval. Maximum (max.) QT, accepted as the longest QT interval, and minimum (min.) QT, accepted as the shortest QT interval, were measured. Measured max. and min. QT intervals were corrected by Bazett's formula (QTc=QT/$\sqrt{}$RR) and were defined as corrected QT interval (QTc) /12). The difference between the max. QTc and min. QTc was defined as QTc dispersion .

Weight loss program

Obese subjects began 12 week weight loss program with orlistat 120 mg three times daily with a mildly reduced calorie diet (1200-1600 kcal/day). The prescribed diet contained approximately 30% of calories from fat, 50% from carbohydrate and %20 from protein. The patients received dietary advice from a qualified dietician. Subjects were invited to regularly control visits at the end of every one month of the weight loss program. The study protocol was approved by the local Ethics Committee, and informed written consents were obtained from each patient at the start of the study.

Statistical Analysis

SPSS 11.0 software (Chicago, II, USA) was used for statistical analysis. Continuous variables were expressed as mean values ± SD. Correlations were performed using Spearman's correlations analysis. The unpaired t test was used for comparison of continuous variables before and after weight loss program. P value <0.05 was considered statistically significant.

Results

Mean age of obese subjects was 44±8 years (range 31-62 years). Hypertension (HT) and diabetes mellitus (DM) were present in 7 (23%) and in 3 (10%) patients, respectively. Seven of the subjects were taking an angiotensin converting enzyme inhibitor or angiotensin-II receptor blocker, 2 of the subjects were taking diuretic treatment, 3 of the subjects were taking calcium channel blockers and 3 of the subjects were taking metformine treatment. After 12 week weight loss program, systolic and diastolic blood pressures, and fasting blood glucose levels of subjects were significantly decreased. Lipid values did not statistically change (Table 1). The BMI decreased from 42±5 kg/m2 to 36±4 kg/m^2 (p<0.001) and mean weight of obese subjects decreased from 110±17 kg to 95±15 kg (p<0.001). The mean amount of weight loss was 14.5±5.0 kg (range 9-32 kg). The average percent of weight loss was 13% (range 10.0%-20.3%).

Electrocardiographic values before and after weight loss are shown in Table 1. Maximum QTc interval (p=0.024) and QTc dispersion (p=0.024) significantly decreased after weight loss program (Fig. 1 and 2, respectively). Whereas, minimum QTc interval slightly increased, but it was not statistically significant (p>0.05) (Fig. 3). A statistically significant correlation (r=0.487, p=0.007) was found between decrease in level of QTc dispersion and amount of weight loss.

The subjects were separated into two groups according to percentage of weight loss. Group 1 (16 subjects); with <12% loss of their original weight and Group 2 (14 subjects); with ≥12% loss of their original weight. The decrease in level of QTc dispersion was more prominent in Group 2 than in Group 1 after weight loss program, though it was not statistically significant (19±23 ms vs 3±26 ms, p>0.05, respectively).

Discussion

The main findings of this study are that (1) substantial weight loss in obese subjects is associated significantly with the decrease in QTc dispersion and (2) decrease in value of QTc dispersion is significantly correlated with the amount of weight loss.

Obesity alone has been found to be a strong predictor of sudden cardiac death (SCD) in the Framingham heart study (13). It

has been suggested that sudden deaths and/or ventricular arrhythmias may be linked to abnormalities in ventricular repolarization (14,15). Increased heterogeneity of ventricular repolarization favors the development of malignant ventricular arrhythmias, and increased QTc dispersion may reflect this inhomogeneity. Obesity may be associated with early electrocardiographic and/or echocardiographic abnormalities even in the absence of clinical symptoms (16,17). Previous studies have been reported that prolongated QTc interval may return to normal range after substantial weight loss in obese subjects (9-11). QTc dispersion is a more sensitive and useful predictor of ventricular arrhythmias and SCD than QTc interval prolongation (15,18). Decrease in level of QTc dispersion after substantial weight loss in this population is unclear. Mshui et al. (19) have reported that QTc intervals (max. and min. QTc interval), except QTc dispersion, decreased after weight loss. In contrast, Grupta et al. (20) reported decrease in level of QTc dispersion in most patients using liquid protein diet for weight loss, and suggested that increase of the minimum QT interval was the cause of the QT dispersion reduction after weight loss. Our findings were similar to results found by Grupta et al. (20). We found significant decrease in level of QTc dispersion after substantial weight loss with medical treatment (orlistat) and diet.

The morbid obesity causes some changes in cardiac morphology such as left ventricular (LV) enlargement, eccentric left (LV) and right ventricular hypertrophy (21,22). Therefore, abnormalities of ventricular repolarization secondary to cardiac structural changes in obese subjects could result in increased sudden deaths and ventricular arrhythmias. Substantial weight loss in morbidly obese subjects produces a variety of favorable cardiac hemodynamic, structural alterations, and ECG changes (23-25).

Table 1. The clinical and electrocardiographic changes before and after weight loss

	Before weight loss (n=30)	After weight loss (n=30)	P
Weight, kg	110±17	95±15	<0.001
BMI, kg/m2	42±5	36±4	<0.001
Systolic blood pressure, mmHg	140±22	129±19	<0.001
Diastolic blood pressure, mmHg	86±10	82±11	<0.001
Fasting glucose, mg/dl	108±17	104±16	<0.001
Total cholesterol, mg/dl	211±36	210±34	0.959
Triglyceride, mg/dl	143±48	118±35	0.264
HDL cholesterol, mg/dl	47±14	50±11	0.206
LDL cholesterol, mg/dl	142±48	147±46	0.773
Heart rate, beats/minute	77±16	76±17	0.586
PR interval, ms	156±16	156±15	0.918
QTc interval, ms	417±18	410±17	0.097
Maximum QTc interval, ms	446±19	433±27	0.024
Minimum QTc interval, ms	380±21	381±22	0.735
QTc dispersion, ms	66±19	52±25	0.024

Mean±SD, BMI- body mass index, HDL- high density lipoprotein cholesterol, LDL- low density lipoprotein cholesterol

These include, reductions in systolic blood pressure and LV end-systolic wall stress, decreases in elevated central blood volume and cardiac output, a decrease in LV chamber size, improvements in LV diastolic filling and regression of LV hypertrophy (24-26). In addition, improvement of autonomic imbalance (decreased sympathetic activity) (27), decrease of hyperinsulinemia (28) and improvement in relative subendocardial ischemia (29) after weight loss in obese subjects may contribute to decrease in the level of QTc dispersion.

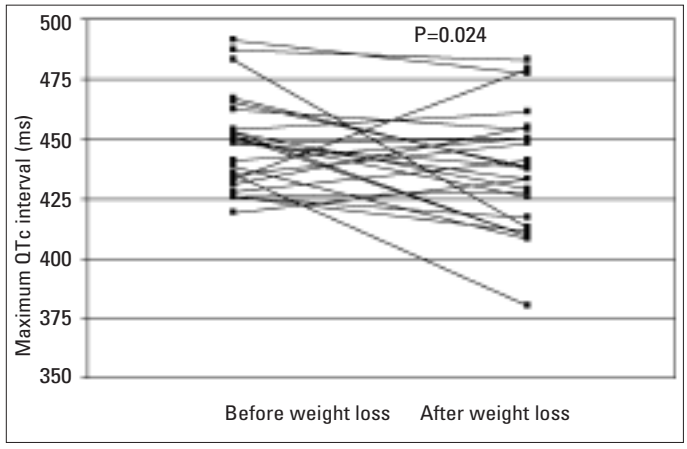

Figure 1. The change of maximum QTc duration before and after weight loss

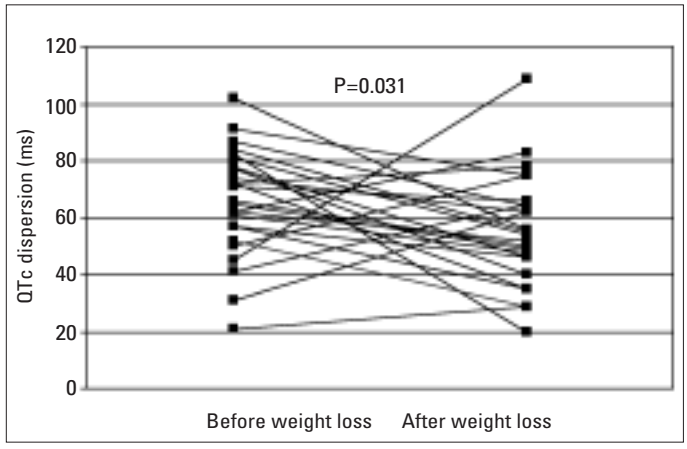

Figure 2. The change of QTc dispersion before and after weight loss

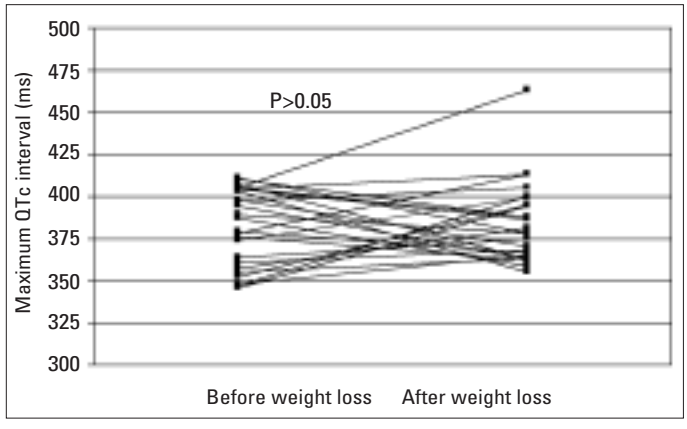

Figure 3. The change of minimum QTc duration before and after weight loss

To our knowledge, there is no any data about the effect of orlistat treatment on ventricular repolarization parameters. However, it has been reported that in combination with a mildly reduced-calorie diet, orlistat significantly reduces body weight, and improves glycaemic control and cardiovascular risk factors in overweight and obese subjects with type 2 DM (30). Therefore, medical therapy such as orlistat may have additional contribution beyond-weight loss on QTc dispersion. It has been demonstrated that ECG repolarization parameters are related to the presence of arterial hypertension, systemic blood pressure, and blood glucose levels, and left ventricular mass (31,32). Therefore, the decrease in blood pressure and fasting glucose levels may contribute to improvement of ventricular repolarization abnormalities in the current study. We did not measure left ventricular mass, insulin resistance and neurohumoral parameters. However, further studies are needed to investigate the causes of regression of QTc dispersion after weight loss by using various methods (echocardiography, heart rate variability, neurohumoral parameters).

We concluded that QTc dispersion is significantly decreased by at least 10% loss of their original weight in obese subjects. It is closely associated with amount of weight loss. Therefore, the results of this study suggested that substantial weight loss may contribute to improvement of the hemodynamic and electrocardiographic abnormalities in obese subjects.

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