Measurement of The QT Dispersion In Patients With Cardiac Syndrome X For The Investigation of Ischemia As An Etiological Factor

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ABSTRACT

Clinical and demographic characteristics of the groups such as age, gender body mass index, systolic and diastolic blood pressure showed no statistically significant differences between both groups. Although there was no difference in QTd values between groups at baseline (43,28 ± 12,55 msec in the positive ETT group, and 40,28 ± 11,08 msec in the control group, p=NS), peak exercise QTd was much higher in the positive ETT group than the control group (57,40 ± 13,70 msec and 28,23 ± 5,05 msec, respectively, p< 0.01). Since QTd greater than 60 msec related to ischemia has been previously reported, ETT positive patients were reevaluated in two different subgroups with QTd ≥ 60 msec (34 patients), and QTd < 60 msec(32 patients). The sum of ST depression were much more in the QTd ≥ 60 msec group (7,22 ± 0,74 vs 4,40 ± 1,78; t: -8,458, p<0.001).

Conclusions: As a result, peak exercise QTd have been found to be higher in the group of patients with CSX than the control group, and especially when peak exercise QTd ≥ 60 msec, ischemia due to microvascular dysfunction or spasm must be considered as one of the leading causes of chest pain.

Key Words: Cardiac syndrome X, QT dispersion, ischemia, exercise treadmill testing.

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ÖZET

Kardiyak Sendrom X Hastalarında Etiyolojik Bir Faktör Olarak İskeminin Araştırılmasında QT Dispersiyonu Ölçümü

Amaç: Pozitif egzersiz testi ile birlikte angina ya da angina benzeri göğüs ağrısı ve normal koroner anjiografi ile karakterize kardiyak sendrom X'in (KSX) gerçek nedeni tartışmalıdır. QT dispersiyonu (QTd) ölçümü miyokard heterojenitesini gösteren invazif olmayan bir yöntemdir. İskemik miyokardın iskemik olmayan miyokardla repolarizasyon süresi farkı QTd'de uzamaya yol açar. Bu çalışmanın amacı KSX'li hastalarda QTd ölçümü ile etyolojik bir faktör olarak iskemi varlığının araştırılmasıdır.

Yöntem: Stabil angina pektorisi olan 105 hasta çalışmaya dahil edildi. Toplam 105 hastanın 66'sı (38 kadın, 28 erkek, ortalama yaş: 48,08±10,21) pozitif egzersiz testi ve normal koroner anjiografi ile KSX olarak teşhis edildi. 39 hastadan oluşan kontrol grubu (24 kadın, 15 erkek, ortalama yaş: 50,84±11,34) ise negatif egzersiz testi ve normal koroner anjiografiye sahipti. QT intervali istirahat ve zirve egzersiz sırasında alınan standart 12 derivasyonlu elektrokardiyografi üzerinden ölçüldü. QTd maksimum

ve minimum QT intervalleri arasındaki farktır. QTd pozitif egzersiz testi ile kontrol grupları arasında karşılaştırıldı.
Bulgular: Gruplar arasında yaş, cinsiyet, vücut kitle indeksi, sistolik ve diyastolik kan basıncı gibi klinik ve demografik özellikler açısından fark saptanmadı. Başlangıçta gruplar arasında QTd değerleri farklı değilken (pozitif egzersiz testi grubunda 43,28 ± 12,55 msn, ve kontrol grubunda 40,28 ± 11,08 msn, p=NS), zirve egzersiz QTd değeri pozitif egzersiz grubunda kontrol grubuna göre daha yüksekti (sırasıyla 57,40 ± 13,70 msn ve 28,23 ± 5,05 msn, p< 0.01). 60 msn'nin üzerindeki QTd değerlerinin iskemi ile ilişkili olduğu daha önceden gösterilmiş olduğundan pozitif egzersiz testi olanlar QTd değerlerine göre <60 (32 hasta) ve ≥60 msn (34 hasta) olarak tekrar değerlendirildi. ST depresyonu toplamı QTd≥60 msn olan grupta daha fazla saptandı (7,22 ± 0,74 vs 4,40 ± 1,78; t: -8,458, p<0.001).
Sonuç: Sonuç olarak KSX'li hastalarda, zirve egzersiz QTd değeri kontrol grubuna gore daha yüksek bulundu. Özellikle zirve egzersiz QTd ≥ 60 msn olduğu durumlarda göğüs ağrısının önde gelen sebebi olarak mikrovasküler disfonksiyon ya da spazma bağlı iskemi dikkate alınmalıdır.
Anahtar Kelimeler: Kardiyak sendrom X, QT dispersiyonu, iskemi, egzersiz treadmill testi.

INTRODUCTION

The term 'cardiac syndrome X (CSX)' is often used to define the patients who have angina-like pain on effort, ST-segment depression on an exercise treadmill testing (ETT), and normal coronary arteries at coronary angiography (1). The exact cause of this disease is not definitely clear but mainly microvascular dysfunction, or abnormal pain perception or sensitivity with no identifiable ischemia have been suggested (2-4).

Recent clinical studies have indicated that QT dispersion (QTd), defined as the difference between maximal and minimal QT intervals on a 12-lead electrocardiography (ECG), is a non-invasive method used for measuring heterogenity in the duration of myocardial repolarization and is associated with regional ischemia and wall motion abnormalities (5,6). QTd at rest varies from 30-60 msec in normal subjects (6). In previous studies, a direct relationship between the prolongation of the QT interval and myocardial ischemia, have been reported (7,8). Recently, it has been reported that QTd obtained by exercise ECG increases the diagnostic reliability of ST segment changes (9,10). The aim of our study is to investigate the presence of ischemia as an etiologic factor in patients with CSX by QTd measurement during ETT.

MATERIALS AND METHODS

Patient Selection

We retrospectively evaluated 66 patients (38 female, 28 male), with typical exercise-induced angina pectoris, transient ischemic ST-segment depression (> 1 mm) during ETT with angiographically normal coronary arteries, diagnosed as CSX. In control group, 39 patients (24 female, 15 male) with complaint of angina chest pain without ST-segment depression during ETT and normal coronary angiographies.

Patients with known chronic heart failure, valvular heart disease, diabetes mellitus, systemic arterial hypertension, extracardiac causes of chest pain, or significant renal or hepatic dysfunction were excluded.

Exercise Treadmill Testing

The ETT was performed according to the modified Bruce protocol (Marquette Case 12 equipment) (11). Before testing, all participants were instructed not to eat, drink or smoke for 3 hours before the test. A resting 12-lead ECG was printed before starting the test and then continuously recorded. An ECG print-out was obtained whenever any abnormality was detected and always at the peak of exercise and immediately after the exercise. In addition, an ECG was printed whenever chest pain occurred. Recovery time of ≥2 minutes was usually allowed if no ST-segment changes were present or exercise-evoked ST changes disappeared during this time. In other cases the recovery phase was terminated when ST-segment normalization was achieved and/or the heart rate slowed to <100 beats/minute. Horizontal or downsloping ST-segment depression ≥ 1 mm 60 msec after the J point in three consecutive beats on two or more derivations corresponding to any myocardial wall, was considered as positive ETT (12). Considering all derivations, ST-segment depressions of ≥ 1 mm were summed.

Blood pressure (BP) was measured by the Korotkoff method using a mercury cuff sphygmomanometer. The BP measurements were taken at rest and during the last minute of each exercise stage, including recovery. The ETT was terminated either because of the patient's request to stop, because of moderate to severe angina limiting exercise continuation, complex ventricular arrhythmia (ventricular bigeminy, ventricular runs or ventricular tachycardia), new bundle branch block, physical exhaustion or any other disabling symptom (intermittent claudication, dizziness or dyspnea). The ETT was also discontinued if no abnormal signs and symptoms were present but the patient's heart rate (HR) exceeded 95% of the age-adjusted limit.

Coronary Angiography

Coronary angiography was performed by a femoral approach using the standard Judkins technique. Coronary arteries in left and right oblique planes and cranial and

caudal angles were demonstrated. Coronary arteries were judged as normal on the basis of visual assessment of the absence of any luminal irregularities.

QT Interval Measurement

QT intervals were measured manually, in as many of the 12 leads as possible on the ECG at rest and peak exercise, from the onset of the QRS complex to the end of the T wave , which was the point of intersection between a line tangential to the downstroke of the T wave, and the T-P baseline in the presence of a U wave. QTd was defined as the difference between the maximal and minimal QT interval measurements.

STATISTICAL ANALYSIS

Statistical analysis was performed by using " Independent simple T test ". All results are expressed as the mean±SEM. A p value <0.05 was regarded as significant.

RESULTS

Characteristics of the study population are presented in Table 1. There were no statistically significant differences between the groups in terms of age, sex, body mass index, smoking, systolic blood pressure, and diastolic blood pressure. And, also, heart rate both during rest and peak exercise, QT maximum, QT minimum, and QTD during rest showed no statistically significant differences (Table 2). On the other hand, QT maximum, QT minimum, and QTd during peak exercise were much higher in CSX group than the control group, in which p value was <0.01, <0.05, and <0.01 respectively (Table 2). Since, a direct relationship between the prolongation of the QT interval and myocardial ischemia, have been reported, we reevaluated CSX patients in two groups: QTd <60 msec, and QT≥60 msec. In QT ≥60 msec group, the sum of ST depression during peak exercise was much higher (Figure).

DISCUSSION

Up to 30% of the patients who underwent coronary angiography to evaluate the causes of chest pain have angiographically normal coronary arteries (1). The term, CSX, first used by Kemp et al. in 1973 to describe a group of patients with typical angina and normal coronary angiograms, is now widely used to specify patients with angina-like chest pain, ischemia-like ECG, normal coronary angiograms, and no evidence of coronary spasm (13-15). Chest pain in patients with CSX is usually exertional and have similar properties to that in patients with coronary artery disease (16).

Although the underlying pathophysiology has not been clearly defined, CSX is characterized by two major abnormalities: coronary microvascular dysfunction, and abnormal cardiac pain perception or sensitivity (2-4). The coronary microvascular dysfunction may be associated with either the reduced coronary microvascular dilatory response to variable physiological and pharmacological stimulies (exercise, adenosine, dipyridamole, and atrial pacing) or the increased coronary resistance at rest, or both (17). Endothelial dysfunction, with reduced bioavailability of endogenous nitric oxide and increased plasma levels of endothelin-1, may explain the abnormal behavior of the coronary microvasculature in CSX (3,18,19). On the other hand, increased pain perception is common in patients with CSX. Potassium and adenosine release, as well as abnormalities in the central modulation of pain perception, have been suggested to play a role (20).

QT interval duration reflects regional variations in ventricular repolarization and cardiac electrical instability. QTd predicts ischemia related arrhythmias in patients with ischemic heart diseases (21). The difference in repolarization duration of ischemic myocardium in accordance to non-ischemic myocardium, causes prolongation of QTd (22-23). QTd prolongation measured during peak exercise is correlated with coronary artery disease, as well. A <16 msec increase in QTd during exercise has a 95% negative predictive value in excluding significant coronary artery disease (24). Both having ST depression and QTd >60 msec during ETT, improve the diagnostic power of exercise testing in evaluating coronary heart disease (9). In our study; in CSX group, QTd during peak exercise was much higher than the control group. And also, there was a significant increase in the sum of ST depression during peak exercise in CSX patients with QTd ≥60 msec than QTd <60 msec CSX patients. In previous studies, similar prolongation of QTd was observed in CSX patients among normal subjects (25,26). And also, an increase in QTd was occurred during exercise-induced myocardial ischemia in women with significant coronary artery disease (9).

In conclusion, we exposed that QTd was much higher in CSX patients than the control group. Since all studies have consistently shown that among CSX patients the occurrence of major cardiac events is similiar to age and sex matched healthy controls, we cannot claim the increased incidence of arrhythmia in these patients (27). However, especially in CSX patients having QTd ≥60 msec during exercise, ischemia may be considered as the leading cause of chest pain.

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