·Clinical Research·

QT interval dispersion in the patients with central serous chorioretinopathy

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Abstract

• AIM: To evaluate QT dispersion (QTD) in patients with central serous chorioretinopathy (CSC).

• METHODS: This clinical, comperative, case-control study included 30 patients with CSC at acute phase (Group 1) and 30 age- and sex-matched healthy subjects (Group 2, the control group). From all subjects, a 12-lead surface electrocardiography was obtained. The heart rate (HR), QT maximum (QT_{max}), QT minimum (QT_{min}), QT corrected (QT_c), QTD and T_{mean} were manually measured and analyzed. Student´s *t*-test and Pearson´s method of correlation were used for statistical analysis.

• RESULTS: The patient and control groups were matched for age, smoking status (rate and duration) and gender. There were no significant differences with regard to these among the groups (P>0.05). The participants included 19 men (63.3%) and 11 women (36.7%) in Group 1, 20 men (66.7%) and 10 women (33.3%) in Group 2. QT_{max}, QTD and QT_c were significantly higher than those of healthy controls (P<0.001 for QT_{max}, P=0.01 for QTD and P=0.001 for QT_c). QT_{min}, T_{mean} and HR did not differ significantly between the study groups (P=0.28 for QT_{min}, P=0.56 for T_{mean} and P>0.05 for HR). No significant correlation was found between duration of the disorder and QTD values (r=0.13, P>0.05).

• CONCLUSION: These findings suggest that CSC may be associated with an increase in QTD and that the patients might be at risk for ventricular arrhythmia.

• **KEYWORDS:** central serous chorioretinopathy; electrocardiography; QT dispersion; ventricular arrhythmia
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INTRODUCTION

Central serous chorioretinopathy (CSC) is characterized by serous detachment of the neurosensorial retina and/or the retinal pigment epithelium (RPE) frequently in the macular region [1]. Spontaneous resolution of serous retinal detachment is common in acute CSC with RPE changes while recurrent or chronic detachment is often associated with diffuse retina pigment epitheliopathy, which is resulting in the RPE atrophy and secondary subretinal neovascularization or polypoidal choroidal vasculopathy. Subsequently, CSC may cause persistent visual impairment[2]. Although the pathogenesis of CSC is unknown, it has been considered that the CSC may be due to focal RPE defect or choroidal lobular ischemia and choroidal venous congestion [3-5]. Recent studies have shown the association of CSC with psychological stress; type A personality; glucocorticoid treatment; endogenous hypercortisolism like Cushing's syndrome; systemic hypertension; and pregnancy. Thus, the increased levels of serum catecholamine, or glucocorticoid, or both, have been thought to play a role in the pathogenesis of CSC, in all these conditions[1, 6-8].

Recent studies showed that the protection against sudden death by use of beta-adrenergic antagonists and left upper thoracic sympathectomy confirmed the importance of sympathetic stimulation as a trigger of arrhythmias [9,10]. It has been known that adrenergic antagonists have been also used in the treatment of CSC. Thus, catecholamines play an important role at the development in both CSC and arrhythmia and could exaggerate the preexisting cardiac ritm abnormalities. Although, there is no data in literature, it is possible that CSC is associated with cardiac arrhythmias because of above mentioned tight relation with sympathetic stimulation.

Cardiac arrhythmia such as ventricular fibrillation is one of most important causes of sudden death. Interlead variability of the QT interval (QT dispersion, QTD) detected in standard electrocardiography (ECG) has been proposed as a marker of electrical instability of the heart [11,12]. QTD is defined as the

difference between the longest and shortest QT interval measured in a 12-lead of the surface ECG. QT interval is the time period from the beginning of the Q wave to the return of the T wave to the isoelectric line in an ECG. QTD is markedly increased in patients with long QT Syndrome (LQTS), which has been considered to indicate arrhythmia risk [13] in this disease. Sympathetic nervous stimulation and catecholamines are known to produce QT prolongation and ventricular arrhythmias in familial LQTS[14,15].

QTD reflects regional heterogeneity of ventricular myocardial repolarization. It has been suggested that QTD could be an important indicator of the risk of ventricular arrhythmia[16]. A higher QTD means a higher heterogeneity in ventricular repolarization and the higher the ventricular instability[17]. This may lead to serious ventricular arrhythmias and, consequently sudden cardiac death[18]. To the best of our knowledge, no previous studies have examined the possible relation between QT elongation and CSC. In our study, we aimed to research the possible relation between CSC and cardiac arrhytmia by evaluating the "QT" segments in standard ECG.

SUBJECTS AND METHODS

Subjects This study included 30 patients with active CSC (Group 1), and 30 age- and sex-matched healthy subjects (Group 2). The study was designed as a clinical comperative case-control study and according to Helsinki Declaration and approved by the institutional ethics committee. Informed consents were obtained from the patients and the volunteers.

Methods

Inclusion criteria All participants were free of all medications (also including vasoactive or psychotropic agents) at least in the previous two weeks.

Group 1 included the patients with acute CSC characterized by detachment of the neurosensorial retina caused by accumulation of serous fluid between the photoreceptor outer segments and the RPE in combination with monofocal or multifocal changes in the RPE documented by fundus fluorescein angiography (FFA) and optical coherence tomography (OCT).

The time from the beginning of visual complaints of patients until admitting to our clinic was accepted as the disease duration. A typical acute CSC is characterized with continuation of complaints and/or serous retinal detachment less than 6mo[19].

Group 2 (control group) included same number of healthy subjects (10 females and 20 males; age 42.3 ±8.9y) by matched sex, age, and smoking without exclusion criteria.

Exclusion criteria Patients at inactive, recurrent or chronic phases of disease were not included in the study.

Participants having current or previous a severe cardiac disease (congestive heart failure, myocardial infarction, coronary artery stenosis, cardiomyopathy, valvular heart disease, a pacemaker), hypertension, existence of low ejection fraction and a severe systemic illness (chronic obstructive pulmonary disease, diabetes mellitus, cancer, *etc*) that could influence autonomic functioning were also excluded from study.

Patients with history of previous coronary vascular surgery or intervention and any intraocular surgery, laser photocoagulation or intravitreal injection for CSC were also excluded.

Electrocardiographic recordings, measurements and analysis The electrocardiographic recordings were carried out in the same quiet room during spontaneous breathing, following 10min of adjustment in the supine position in morning hours. From all subjects, a 12-lead surface ECG was obtained. During recordings, participants were not allowed to speak. The ECGs were recorded at a paper at 10 mm/mV amplitude and 25 mm/s rate speed. Three leads were recorded simultaneously. To improve accuracy, all measurements were performed with calipers and magnifying lens for defining the ECG deflection, and the heart rate (HR), QT maximum (QT_{max}), QT minimum (QT_{min}), QT corrected (QT_c), QTD and T_{mean} were manually measured and analyzed by an investigator blinded to the clinical data [20]. These recordings were also analyzed by another investigator to determine the interinvestigator variability.

The QT interval was manually measured by using hand-held calipers from the beginning of the QRS complex to the end of the T-wave in all 12 leads. The end of the T-wave was described as the intersection between a tangent to the terminal slope of the T-wave and the PR baseline. Only monophasic well defined T-waves were accepted for measurement. If the end of the T-wave could not be identified because of the low amplitude of the T-wave, then the lead was excluded from analysis. If a U-wave was present, then a tangential line was drawn on the terminal slope of the T-wave and the end of the T-wave was determined as the point of intersection of this line with the isoelectric base. The QT interval and the preceding RR interval were measured in three consecutive cycles. In each lead mean of the corrected QT_c interval of three consecutive beats was considered as the QT_c interval of that lead[20-22].

The heart rate-corrected QT interval [QT_c, millisecond (ms)] was calculated by using Bazett's formula [$QT_c=QT/\sqrt{(RR)}$] for each derivation. The QT_c (ms) was defined as the absolute difference between the maximum (QT_{cmax}) and minimum (QT_{cmin}) QT_c interval in any of the ECG leads[23]. To determine the intraobserver variability of QT_c interval measurements, 20 randomly selected electrocardiograms were analyzed by the same observer at a different time. These recordings were also analyzed by another observer to determine the interobserver variability.

Statistical Analysis Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 11.0 (SPSS Inc., Chicago, IL, USA). In the statistical analysis, Student's *t*-test and Pearson's method of correlation were used. In addition, analysis covariance (ANCOVA) was used, with HR as covariate. All data are presented as mean± standard deviation (SD). A *P* value less 0.05 was considered as significantly.

RESULTS

Thirty healthy subjects (Group 1) and 30 patients with acute CSC (Group 2) were enrolled in this study. The participants included 19 men (63.3%) and 11 women (36.7%) in Group 1, 20 men (66.7%) and 10 women (33.3%) men in Group 2. The mean ages of the Group 1 and Group 2 were 42.0±6.2 and 42.3±8.9y, respectively. The study groups were matched for age, smoking status (rate and duration) and sex and there were no significant differences with regard to these among the groups (P>0.05). Demographic data of participants in the study groups are demonstrated in Table 1. The mean duration of disease for the patient group was 24.7 ±8.3d. Demographic data of participants in the study groups are summarized in Table 1.

The electrocardiographic data are summarized in Table 1. QT_{max}, QTD and QT_c were significantly higher than those of healthy controls (P<0.001 for QT_{max}, P=0.01 for QTD and P=0.001 for QT_c). QT_{min} and T_{mean} were not showed significantly statistical difference in the patients group than in the controls (P=0.28 for QT_{min} and P=0.56 for T_{mean}). Heart rate did not differ significantly between the groups (P>0.05). No significant correlation was found between duration of the disorder and QTD values (r=0.13, P>0.05, Figure 1). The interobserver variability was less than 5% for all of the electrocardiographic variables.

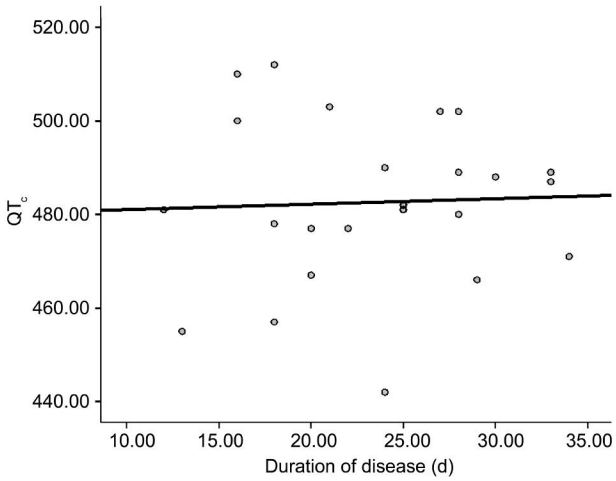

Figure 1 Data of correlation between duration of disorder and QTD values.

Table 1 Demographical data and QT segment measurements of the study groups

Demographical and electrocardiographical data	Patients	Controls	*P*
Mean age (a±SD)	42.0±6.2	42.3±8.9	0.91
Sex ratio (F/M)	19/11	20/10	0.82
Duration of disease (d)	24.7± 8.3	-	-
QT_{max}	434.5±12.5	416.1±11.8	<0.001
QT_{min}	373.1±21.9	366.7±18.4	0.28
QTD	61.3±13.7	49.4±16.5	0.01
QT_c	482.1±17.5	466.1±15.3	0.001
T_{mean}	1.62±0.2	1.65±0.02	0.56
Heart rate (beats/min)	70.9±12.5	71.5±10.9	0.87

DISCUSSION

Although there are various risk factors for the development of CSC, psychosomatic factors and the increased levels of serum catecholamine or both have been thought to have important role in the pathogenesis of CSC. Yannuzzi [1] considered that type A personality might be strongly associated with the sympathetic release in CSC and that macula was the target tissue for this pathology.

In the previous studies, it has been suggested that CSC could be created by intravenous epinephrine in the experimental monkey model [24-27]. It was postulated that elevated catecholamine levels in patients with CSC might cause choroidal vasoconstriction by activating the sympathetic nervous system. It was considered that the elevation of choroidal hydrostatic pressure caused by choroidal vasoconstriction leads to the breakdown of tight junctions among RPE cells, allowing fluid to pass from the choroid to the subretinal space [28]. Previous studies have also demonstrated that CSC patients have some traits such as a neuroticism, emotional instability, introversion and alexithymia, as well as type A behavior. All these personality traits point to emotional disregulation [29-33]. Psychological stress or disorders associated with increased sympathetic nervous system stimulation contribute to the development of CSC as an important risk factor[34-36].

In some studies on QTD in some physiciatric diseases including panic disorder, social fobia and anorexia nervosa, it was considered that QTD might be associated with these disorders [37-39]. Recent clinical studies also demonstrated that the prognostic significance of the QT interval and QTD in the patients with type I DM, carbon monooxyde poisoning, ankylosing spondylitis, electrolyte imbalance, undergoing dialysis, renal transplant and severe burns[40-45].

In many clinical studies on cardiologic patients, it was reported that QTD was a risk factor for arrhythmia and unexpected cardiac death patients with LQTS and chronic heart failure, respectively [12,46,47]. It has been well known that sympathetic nervous stimulation and catecholamines caused QT prolongation and ventricular arrhythmias in familial LQTS[14,15].

QT dispersion reflects regional heterogeneity of ventricular myocardial repolarization and has been suggested as an important indicator of the risk of arrhythmia, in addition to

the QT interval. QT interval refers to the overall duration of the electrical activation and resting of the ventricle, corresponding to the location of each lead, and is inversely correlated with the HR [16]. Normally, QTD is within 40-60ms; if it exceeds 100ms or rises by 100% from baseline, the condition is considered to be pathologic. A higher QTD means a higher heterogeneity in ventricular repolarization and the higher the ventricular instability[17]. Nonhomogeneous conduction velocity in different regions of ventricles, *i.e.* increase in QTD, may lead to serious ventricular arrhythmias and, consequently sudden cardiac death[18, 46, 47].

To our best knowledge, this is the first study which investigated QTD in patients with CSC. In our study, we found that QTD in the patients with CSC were significantly higher than those of healthy controls. Thus, we suggest that QTD may be a marker of CSC and that otherwise; the patients with CSC might be at risk for ventricular arryhthmia and sudden death. However, further studies having large sample number and with long follow-up time, in which QTD values are screened at different phases such as inactive, chronic, recurrent throughout the course of the disorder, are needed to support our opinion.

Our study has some limitations: electrocardiographical measurements were performed using a 10× lens, not using computer programming or automated measurement methods. Electrophysiological evaluation was not performed. The patients were not followed up longitudinally for morbidity and mortality. Finally, in our study, catecholamines, which might associate with CSC, were not evaluated. However, this assessment is difficult because the levels of these hormones may be easily affected by various factors and situations.

In conclusion, QTD detected by ECG, an easily applied non-invasive method may show the risk of ventricular arrhythmia in the patients with CSC. As QTD may be associated with CSC, and the patients with CSC should be closely followed-up because they might be at risk cardiac ventricular arrythmia.

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