Electrocardiographic P Wave Dispersion May Be a Risk Factor for Atrial Arrhythmia in The Patients With Central Serous Chorioretinopathy

Elektrokardiyografik P Dalga Dispersiyonu Santral Seröz Koryoretinopatili Hastalarda Atriyal Aritmi için Bir Risk Faktörü Olabilir

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ABSTRACT

Purpose: The aim of this study was to evaluate electrocardiographic P-wave dispersion (PWD) in patients with central serous chorioretinopathy (CSC).

Materials and Methods: This comparative, case-control study included 40 patients with CSC at acute phase and 40 age- and sex-matched healthy subjects. The heart rate (HR), P maximum (P_{max}), P minimum (P_{min}) and PWD were manually measured and analyzed on a 12-lead surface electrocardiograms.

Results: There were no significant differences with regard to age, smoking status (rate and duration) and gender among the groups (P>0.05). The participants included 22 men (55%) and 18 women (45%) in the patient group, 20 men (50%) and 20 women (50%) in the control group. The mean P_{max}, P_{min}, and PWD in the patient group were significantly higher than those of the control group (p=0. 001, p=0. 01 and p=0. 04, respectively). HR did not differ significantly between the study groups (P>0.05). No significant correlation was found between duration of the disorder and PWD values (r= 0.13, P > 0.05).

Conclusions: Our study suggests that CSC may be associated with an increased PWD and high risk for atrial arrhythmia.

Key words: Central serous chorioretinopathy, electrocardiography, P wave dispersion, atrial arrhythmia, atrial fibrillation.

ÖZ

Amaç: Bu çalışmanın amacı santral seröz koryoretinopati (SSKR)li hastalarda elektrokardiyografik p dalga dispersiyonu(PDD)nu değerlendirmek amaçlandı.

Gereç ve Yöntem: Bu kıyaslamalı, vaka kontrol çalışması akut evredeki 40 SSKR hastasını ve yaş ve cins olarak benzer 40 sağlıklı kişiyi içerdi. Kalp hızı, P maksimum (P_{maks}), P minimum (P_{min}) and PDD 12-derivasyonlu elektrokardiyogramda manuel olarak ölçüldü ve analiz edildi.

Bulgular: Gruplar arasında yaş, sigara içim (miktar ve süre) ve cins açısından anlamlı fark yoktu (p>0.05). Hasta grubundaki katılımcıların 22'si erkek (%55) ve 18'i kadındı (%45); kontrol grubundakilerin 20'si erkek (%50), yirmisi kadındı (%50). Ortalama P_{maks}, P_{min}, ve PDD hasta grubunda control grubundakilerden anlamlı derecede daha yüksekti (sırasıyla, p=0.001, p=0.01 ve p=0.04). Kalp hızı çalışma grupları arasında anlamlı farklılık göstermedi (p>0.05). Hastalık süresi ve PDD değerleri arasında anlamlı korelasyon bulunmadı (r= 0.13, P > 0.05).

Sonuç: Çalışmamız SSKR'nin artmış PDD ve yüksek atriyal aritmi riski ile ilişkili olabileceğini ileri sürmektedir.

Anahtar Kelimeler: Santral seröz koryoretinopati, elektrokardiyografi, P dalga dispersiyonu, atriyal aritmi, atriyal fibrillasyon.

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BACKGROUND

Central serous chorioretinopathy (CSC) is characterized by the serous neurosensory retinal detachment and/or the retinal pigment epithelium (RPE) detachment frequently in the macula.[1] Although it is a self-limiting disease, its recurrence rate is about 30-50%. Spontaneous resolution of serous retinal detachment is common in acute CSC with RPE changes. However, recurrent or chronic detachments are often associated with diffuse retina pigment epitheliopathy and these may result in the RPE atrophy and secondary subretinal neovascularization.[2]

Although the pathogenesis of CSC is unknown, it has been considered that the CSC may be due to focal RPE defect or lobular ischemia and venous congestion in the choroid.[3-5] It has been demonstrated that CSC might be associate with psychological stress, type A personality, glucocorticoid treatment, endogenous hypercortisolism, systemic hypertension and pregnancy, and that the high serum catecholamine or glucocorticoid levels might 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.[11, 12] Thus, catecholamines play an important role in the development of both CSC and arrhythmia and could exaggerate the preexisting cardiac rhythm abnormalities. Although there is no data in the literature, it is possible that CSC is associated with cardiac arrhythmias because of the above mentioned tight relation with sympathetic stimulation. Atrial arrhythmia is one of the most important causes of sudden death. Standard electrocardiography (ECG) is a clinically available method to detect atrial rhythm abnormalities.[13, 14] P-wave dispersion (PWD), defined as the difference between the maximum and the minimum P-wave (Pmax and Pmin, respectively) are ECG markers that have been used to evaluate the discontinuous propagation of sinus impulses and the prolongation of atrial conduction time, respectively. Prolonged P-wave duration and increased PWD have been reported to be related to increased risk for atrial fibrillation (AF). Some investigators proposed that it may be a predisposing factor for arrhythmic events and sudden death.[13-15]

To the best of our knowledge, there is no previous study regarding the possible relation between PWD and CSC. In our study, we aimed to research the possible relation between CSC and cardiac arrhythmia by evaluating the P wave segments in standard electrocardiography.

MATERIALS AND METHODS

This study was designed as a clinical comparative case-control study and included 40 patients with active CSC (Group 1), and 40 age- and sex-matched healthy subjects (Group 2). The study was designed according to Helsinki Declaration and approved by the institutional ethics committee. Informed consents were obtained from the patients and the volunteers.

All participants were free of all topical or systemic medications (also including antibiotics, vasoactive or psychotropic agents that could influence ECG findings) at least in the previous two weeks.

Group 1 (Patients' group) included the patients with CSC in the acute phase characterized by a detachment of the neurosensory retina caused by accumulation of serous fluid between the photoreceptor outer segments and the RPE in combination with mono focal 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 phase of CSC is characterized by continuation of complaints and/or serous retinal detachment less than 6 months.[16]

Group 2 (Control group) included the same number of healthy subjects (20 female and 20 male; mean age 40.6±6.1years) 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 (severe respiratory tract infection, chronic obstructive pulmonary disease, diabetes mellitus, cancer, etc.) that could influence autonomic functioning were also excluded from the study. Patients with a history of previous coronary vascular surgery or intervention and any intraocular surgery, laser photocoagulation or intravitreal injection for CSC were also excluded.

The electrocardiographic measurements and assessments

The electrocardiographic recordings were carried out in the same quiet room during spontaneous breathing, following 10 minutes of adjustment in the supine position in the 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), P-wave du-

rations and PWDs were manually measured and analyzed by an investigator blinded to the clinical data.[17-19] These recordings were also analyzed by another investigator to determine the interinvestigator variability. The onset of P wave was defined as the junction between the isoelectric line and the start of P wave deflection, and the offset of the P-waves as the junction between the end of the P wave deflection and the isoelectric line.[17, 19] P_{max} in any of the 12-lead surface ECG was calculated and used as a marker of prolonged atrial conduction time. PWD, defined as the difference between P_{max} and P_{min}, was calculated from the 12-lead ECG. To determine the intraobserver variability of P-wave measurements, 20 randomly selected electrocardiograms were analyzed by the same observer at a different time.

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 heart rate (HR) as a covariate. All data are presented as a mean ±standard deviation (SD). A P value less 0.05 was considered as significantly. These recordings were also analyzed by another observer to determine the interobserver variability. In addition, the power analysis was used to calculate the sample size determination of our study population and it was estimated that a population consisting of about 13 patients to be enough. However, we decided to include 40 subjects in each group with the value of %90 power of the study.

RESULTS

The participants included 22 men (55%) and 18 women (45%) in the patient group, 20 men (50%) and 20 women (50%) men in the control group. The mean ages of the patients and controls were 41.4±7.3 and 40.6±6.1 years, respectively. The study groups were matched for age, smoking status (rate and duration) and sex, and there were no significant differences with regard to those among the groups (P>0.05). The mean duration of disease in for the patient group was 19.8± 10.7 days. Demographic and electrocardiographic data of subjects in the study groups are summarized in Table 1.

Table 1. Demographical data and P-wave measurements of the study groups.

	Patients	Controls	*p* value
Mean age (Year±SD)	41.4±7.3	40.6±6.1	0.56
Sex ratio (Female/Male)	18/22	20/20	0.72
Duration of disease (day)	19.8± 10.7	-	-
P_{max}	101±12.5	89.9±9.7	0.001
P_{min}	71.1±10.1	64±9.1	0.01
PWD	29.8±7.3	25.9±7	0.04
Heart rate (beats/min)	72.9±9.7	74.2±11.1	0.76

The mean P_{max}, P_{min}, and PWD in the patient group were significantly higher than those of the control group (p=0. 001 for P_{max}, p=0.01 for P_{min} and p=0.04 for PWD). HR did not differ significantly between the study groups (P>0.05). No significant correlation was found between duration of the disorder and PWD values (r= 0.13, P > 0.05). The interobserver variability was less than 5% for all of the electrocardiographic variables.

DISCUSSION

Central serous chorioretinopathy was demonstrated to be associated with psychosomatic factors, the increased levels of serum catecholamine and psychological stress. Yannuzzi considered that Type A personality might be strongly associated with the sympathetic release in CSC.[1] Additionally, it has been reported that CSC could be created by intravenous epinephrine in the experimental monkey model.[20-23] 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.[4, 12, 23]

Previous studies have also demonstrated that CSC patients have emotional dysregulation and some psychosomatic disorders such as neuroticism, emotional instability, introversion, and alexithymia.[1, 24-30] Psychological stress or disorders associated with increased sympathetic nervous system stimulation contribute to the development of CSC as an important risk factor.[12, 25-31] In recent studies, it was considered that PWD might be related to some physiatric diseases, including panic disorder and hypochondriasis.[32, 33] PWD is defined as the difference between maximum and minimum values of P-wave duration. It is considered that PWD is related to the nonhomogeneous and discontinuous propagation of sinus impulses through the atrial wall. Prolonged P-wave duration and increased PWD have been reported to be related to increased risk for atrial fibrillation (AF). The prolongation of P-wave duration is an accepted indicator of a disturbance in the interatrial conduction and is depicted as a prolonged P-wave (>110 msec) on an electrocardiogram.[13-16] There are some studies demonstrating significant associations between PWD and cardiac autonomic imbalance.[34-40] It was reported that increased sympathetic activity causes a significant increase in PWD.[34]

Additionally, it is well known that there is a tight relation between sympathetic overstimulation and CSC.[1, 8, 12, 21, 22] Therefore; increased PWD in patients with CSC might be partly related to an elevation in sympathetic activity. Recent clinical studies also demonstrated that the PWD duration increased in some chronic inflammatory diseases with the autoimmune origin, such as Behçet Disease, polycystic ovary syndrome, and lichen planus.[41-43] It has been suggested that

prolongation of P-wave duration is an accepted indicator of an interatrial conduction disturbance.[13, 16, 19, 37-40] In addition, it has been suspected that prolongation of P-wave duration might be caused in part by abnormalities inner atrial electrical properties, such as intra-atrial or interatrial conduction disturbance or block.[41-43] These studies support the notion that PWD prolongation may be associated with sympathetic overstimulation. In a recent study, we had reported that CSC might be associated with an increase in QT dispersion and that the patients with CSC might be at risk for ventricular arrhythmia.[44] To our best knowledge, this is the first study in which PWD was investigated in patients with CSC. In the current study, we also found that PWD in the patients with CSC was significantly higher than those of healthy controls. Thus, we suggest that PWD may be a marker of CSC and that otherwise; the patients with CSC might be at risk for cardiac arrhythmias such as atrial fibrillation and sudden death. However, further studies having large sample number and with longer follow-up time, in which PWD 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: Electrocardiographically measurements were performed using a 10x lens, not using computer programming or automated measurement methods. The 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, our study suggests that PWD detected by ECG, an easily applied non-invasive method might show the risk of atrial arrhythmia in the patients with CSC. As PWD may be associated with CSC, and the patients with CSC should be followed-up because they might be at risk cardiac arrhythmia.

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Authors' contributions

Study concept and design: BT and ND; acquisition of data: SGK, ND, RT and OD; analysis and interpretation of data: BT, ND, OD and MK; drafting of the manuscript: BT; critical revision of the manuscript: BT. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

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