Research Article

P wave dispersion in patients with premenstrual dysphoric disorder

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Abstract

**Background:** Growing evidence has revealed that fear and anxiety related situations could affect cardiac parameters. P wave dispersion (Pd) is an important index. In the present study, we aimed to evaluate Pd values in patients with premenstrual dysphoric disorder.

**Methods:** The study was composed of twenty-five female patients with premenstrual dysphoric disorder and same number of healthy controls. Pd, Pmin and Pmax values were determined by electrocardiogram (ECG) in the subjects.

**Results:** It was found that patients with premenstrual dysphoric disorder had considerably higher Pmax and Pmin values compared to those of healthy subjects. Pd was also significantly higher in patients with premenstrual dysphoric disorders than that of healthy subjects.

**Conclusion:** Study suggests that patients with premenstrual dysphoric disorder seems to have increased Pd, as can be seen in anxiety and fear related clinical conditions, considering that this group of patients have an increased trend to cardiac abnormalities, particularly cardiac arrhythmias. To access strong conclusion, it is required novel studies with larger samples.

Introduction

Premenstrual syndrome (PS) is a clinical manifestation in which a series of physical, mental, and behavioral changes emerge in the late luteal phase of the menstrual cycle in women and in which this situation passes generally with the start of menstrual bleeding [1]. Irritability, sensitivity, bursts of anger, states of depression, and anxiety are the most frequently encountered mental symptoms. Approximately 70%-90% of women of reproductive age describe premenstrual symptoms at light or moderate severity, while 3%-8% report high severity [2].

Even though hypothalamic-pituitary hormones are more discussed the cause of this disease is not fully known yet. The preeminent view in the hormonal etymology of premenstrual syndrome such that the disease leads to the emergence of clinical findings by triggering the central neurochemical incidents of normal cycle fluctuations in gonadal hormones in women prone to this situation [3]. Psychosocial stress factors can increase the severity of the symptoms of the disease by producing psychiatric symptoms like anxiety and depression in patients. The relationship between depression and the hypothalamus pituitary adrenal axis (HPA) has been known for a long time [4].

The hypothalamus pituitary adrenal axis activates first after stress, and the corticotropin releasing hormone (CRH) and arginine-vasopressin (AVP) are secreted from the hypothalamus [5]. CRH and AVP lead to the secretion of the adrenocorticotropic hormone (ACTH) and endorphins from the anterior pituitary and, as a result, to the secretion of glucocorticoid from the adrenal cortex[6]. The hyperactivity of the HPA axis causes increased activity in the sympathetic adrenal system by means of centrally regulating mechanisms and, as a result, an increase in the levels of plasma catecholamine. The complicated effects over the endocrine system of depression prepare a setting in which cardiovascular diseases are triggered [5,6]. Beta adrenergic stimulation facilitates the formation of AF by reducing the duration of action potential.
(AP) both with its direct effect over the myocardium and with its indirect effect on the heart rate or the cholinergic system [7].

Anxiety, irritability, and depression are the most frequently encountered psychiatric symptoms in premenstrual syndrome. A significant increase occurs in symptomatic activity in this patient group after a stress response triggered by behavioral and psychiatric symptoms. Increased symptomatic activity can create a risk factor for almost all cardiovascular patients, including those with arrhythmia. The most frequently seen type of arrhythmia in the cardiology literature is atrial fibrillation (AF). AF is a type of supraventricular arrhythmia that emerges if combined atrial contractions have entirely dissipated. It has been reported that the P wave dispersion is a sensitive and specific precursor to AF in various clinical circumstances and can be used as an indicator for paroxysmal atrial fibrillation (PAF) [8-10]. P wave dispersion is defined as the difference between the longest and shortest P wave recorded from different surface electrocardiogram derivations [8,9]. There are a limited number of studies that research the relationship between anxiety disorder and P-wave dispersion (Pd), accepted in the cardiology literature as an indirect indicator of AF. No study was found in which patients with PS, of whom 80% are accompanied by findings of anxiety, are compared with a healthy control group.

Our study aims to recognize the patients at risk for arrhythmia by taking electrocardiography (ECG), which is a noninvasive and inexpensive procedure in patients diagnosed with PS, and to be able to preclude the arrhythmia that may subsequently occur as a result of the consultation with cardiology. Thus, an additional aim is to be able to effectively maintain psychiatric treatments and to reduce the potential risk of arrhythmia.

Methods and Materials

Study population

Twenty-five patients with PS who were referred on foot to the Firat University Faculty of Medicine Hospital Maternity Clinic or are receiving inpatient treatment were included in the study. Patients were sought on the condition of not using any vasoactive or psychotropic agents, not having any kind of heart disease, and not using any alcohol or other substances. Again, patients were sought on the condition of having a resting blood pressure under 120/80 mmHg and having a left ventricular ejection fraction rate above 50%. Twenty-five individuals were included in the health control group with sociodemographic characteristics similar to the patient group. In all cases, a Sociodemographic and Clinical Data Form were prepared with consideration of the purposes of the study. The P dispersion was later calculated for all participants with a 10x lens by the cardiology doctor by taking 12-derivation ECGs. The ECGs of both groups were taken in the morning hours with an ECG device set to a speed of 50 mm/s with 12 derivations after lying down and relaxing in a quiet room for 10 minutes.

Statistical analysis

All values are shown as mean ± standard deviation (SD), and analyzed using Student’s t test. The chi-square test was used to compare categorical variables. All data were evaluated by SPSS for Windows 16.0 (SPSS/PC, 1998). Correlation analysis was performed by Spearman Rank correlations test. Differences were considered significant at $p < 0.05$ for all these tests.

Results

We did not determine any considerable differences with respect to age distribution, or other sociodemographic variables between patients with premenstrual dysphoric disorder and healthy control subjects, as can be seen in table 1. Apart from this, we did not observe any difference in regard to nutritional habits or smoking rate between groups ($p > 0.05$).

One of main finding of the study was that patients with premenstrual dysphoric disorder had considerably higher Pmax values compared to those of healthy comparisons ($88.19 ± 4.56$ ms for patients with premenstrual dysphoric disorder versus $75.50 ± 3.06$ ms for healthy ones, $p < 0.001$). There was also a significant difference for Pmin between groups ($44.71 ± 2.80$ ms for the patient group versus $42.00 ± 2.48$ ms for control group, $p < 0.001$). When measured main parameter of the study, we seen that Pd was significantly higher in patients with premenstrual dysphoric disorders than that of healthy comparisons ($p < 0.001$) ($43.47 ± 5.85$ ms for patients versus $33.50 ± 4.26$ ms for healthy controls. No correlational relationship existed between Pmax, Pmin, or Pd, and sociodemographic variables ($p > 0.05$).

Discussion

This is the first study evaluating Pd in patients with premenstrual dysphoric disorder. The main findings of the present study were: (i) patients with premenstrual dysphoric disorder had considerably higher Pmax values compared to those of healthy subjects (ii) there was also a significant difference for Pmin between groups; (iii) Pd was significantly higher in patients with premenstrual dysphoric disorders than

| Table 1: Participants characteristics and P wave dispersion, Left atrium and Ejection fraction values. |
|---------------------------------------------------------------|
| **Age (range)** | **Ppatients (n = 25)** | **Controls (n = 25)** | **p value** |
| Age (range) | 28.76 ± 3.95 | 26.88 ± 2.36 | $P > 0.05$ |
| Pmax | 88.19 ± 4.56 | 75.50 ± 3.06 | $P < 0.001$ |
| Pmin | 44.71 ± 2.80 | 42.00 ± 2.48 | $P > 0.01$ |
| Pd | 43.47 ± 5.86 | 33.50 ± 4.25 | $P < 0.001$ |
| LA size | 38.47 ± 5.85 | 36.50 ± 4.26 | $P > 0.05$ |
| EF | 60.22 ± 5.27 | 61.71 ± 3.34 | $P > 0.05$ |

Y-BOCS = Yale-Brown Obsession Compulsion Scale; F = Female; M = Male; Pd: P wave dispersion; LA: Left atrium; EF: Ejection fraction. The values are the mean ± SD (range).
that of healthy subjects ($p < 0.001$). The relationship between the association between anxiety and autonomous nervous system seems to be well-established so far. However, there have not been enough studies on anxiety disorders in which cardiac parameters were evaluated. In this context, Nahshoni et al. [11] examined QT dispersion in 16 physically healthy and non-depressed outpatients with long-term social phobia and in 15 healthy controls and determined that patients with social phobia had considerably higher QT dispersion (QTd) and rate-corrected QTd values compared to that of healthy controls, and implicated that QTd values were highly correlated with the two Liebowitz Social Anxiety Scale sub-scores. Our study group also evaluated ECG parameters in a variety of anxiety and anxiety-related disorders. In association with this, we previously examined Pd in 30 outpatients with panic disorder and in 30 physically and mentally healthy age- and gender-matched controls and detected that both Pmax and Pmin were significantly higher than those of healthy controls and Pd was found significantly greater in the panic disorder group than the controls, as was the rate-corrected Pd [12]. In another study, we investigated a total of 25 patients with obsessive-compulsive disorder (OCD) and same number of physically and mentally healthy age- and gender-matched controls and determined that Pmax and Pd were significantly higher in patients with OCD compared to controls whereas Pmin did not differ between groups, with a finding revealing that Y-BOCS scores for the patient group was positively correlated with Pd [13]. In another study, our study group found that another anxiety and fear related clinical condition vaginismus patients had significantly higher Pd values compared to those of healthy control subjects, indicating that anxiety related situations were closely related to cardiac parameter alterations including Pd and were more sensitive to cardiac abnormalities such as arrhythmias (unpublished study). It was also examined Pd in patients with hypochondriasis [14]. It was determined patients with hypochondriasis to have significantly higher Pmax and Pmin values compared to those of healthy control subjects, and to have considerably longer corrected Pd values than healthy ones, considering that hypochondriac patients might have increased risk for cardiac arrhythmias. When taking into consideration that hypochondriasis is an anxiety related condition, our present results led us to consider that premenstrual dysphoric disorder seems to be related to increase PD and indirectly increased risk for arrhythmias. But, when taking into consideration that this is first and limited sampled study, longitudinal studies with larger sample are required.

When reading the present study, some important limitations should be taken into consideration. First of all, we should implicate that our sample size of the present study was small. For this reason, future studies with larger sample are required. Secondly, we only evaluated some cardiac parameters themselves. We did not examine related cardiac, hormonal, or other biochemical variables. Third, we also did not examine the patients with premenstrual dysphoric disorder outside this period with electrocardiographic findings with transient or permanent.

Finally, we suggest that patients with premenstrual dysphoric disorder seems to have increased Pd, as can be seen in anxiety and fear related clinical conditions, considering that this group of patients have an increased trend to cardiac abnormalities, particularly cardiac arrhythmias. To access strong conclusion, it is required novel studies with larger sample.

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