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Preeclampsia as a cardiovascular risk factor

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Abstract

Preeclampsia, the leading cause of maternal and perinatal morbidity and mortality, has been recently considered not only a pregnancy disease but also a risk factor for developing diseases later in life. We aimed to assess the electrocardiographic interval between the peak and the end of the electrocardiographic T wave (Tp–e), Tp-e/QT ratio and Tp–e/corrected QT (QTc) ratio as candidate markers of ventricular arrhythmias in patients with history of preeclampsia. Total of 29 patients with a history of preeclampsia and 30 controls were enrolled in the present study. Cardiometabolic risk markers were compared in women with prior history of preeclampsia vs. uncomplicated term births. Fasting lipids, blood pressure (BP) and inflammatory markers measured and electrocardiogram (Tp-e interval, Tp-e/QT, and Tp-e/ QTc ratios) results evaluated at least 12 months after delivery. QT interval (371.9± 39.2 vs. 353.0±21.1; p=0.001), QTc interval (398.8±39.5 vs. 364.4±31.1; p=0.03), Tp-e interval (66.2±10.6 vs. 41.5±5.1; p<0.001), Tp-e/QT ratio (0.17±0.06 vs. 0.11±0.01; p<0.001) and Tp-e/QTc ratio (0.17±0.09 vs. 0.12±0.01; p=0.003) were signicantly higher in patients with a history of preeclampsia than control group. The results of the present study showed that Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios were greater in patients with a history of preeclampsia.

Keywords: Preeclampsia, ventricular repolarization, Tp-e interval, Tp-e/QT ratio

Introduction

As one of the major causes of maternal mortality across the world, preeclampsia affects 2-8% of all pregnancies. It is a pregnancy syndrome characterized by hypertension occurring after the twentieth gestational week, general maternal endothelial dysfunction, and other probable serious complications [1]. Although the clinical signs of the disease typically start to abate after birth, recent opinion suggests that preeclampsia is no longer limited to pregnancy [2-6]. Linked to increased risk of cardiovascular disease (CVD) including arrhythmia in the later years of the mother, preeclampsia has been accepted as an independent gender-specific CVD risk factor by the American Heart Association [7].

Cardiac arrhythmia includes a broad and heterogeneous group of the heart's electrical abnormalities with or without the presence of an underlying structural heart disease and the primary mean of analyzing arrhythmia is electrocardiography (ECG) [8]. Non-specific ECG changes are used to estimate the morbidity and mortality of a future cardiovascular disease (CVD) [7,8].

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The electrocardiographic ventricular repolarization markers used to predict cardiac arrhythmia include electrocardiographic QT interval time, QT dispersion (the difference between the maximum and minimum QT times), Tp-e interval (the interval between the peak and the end of the T-wave) and Tp-e/QT ratio. It has been argued that these markers can be used to identify patients with a high risk of ventricular arrhythmia [9-12].

The purpose of this study is to assess ventricular repolarization using QT interval time, QT dispersion, Tp-e interval, and Tp-e/QT ratio in patients with a history of preeclampsia.

Material and Methods

Study group

This single-center prospective study included 59 subjects with full-term pregnancy; 29 with a history of preeclampsia and 30 healthy women, matched for age and body mass index, who had a delivery at least 12 months ago, and were from those who consecutively presented to the Postgraduate Training and Research Hospital for a check-up between September 2016 and May 2017.

The basic demographic and clinic characteristics of the study population were reviewed. The study complied with the principles mentioned in the Helsinki Declaration and was approved by the

institutional Clinical Study Assessment Committee of this hospital.

The exclusion criteria of the study were: coronary heart disease or apparent heart valve disease, decompensated heart failure, decreased functioning of the left ventricle (LV) [LV ejection fraction (LVEF) < 50%], complete or incomplete bundle branch block, ST-T abnormalities, atrial fibrillation, use of drugs that may affect Tp-e or QT intervals, resistant or uncontrolled hypertension, LV concentric hypertrophy, or presence of evidence indicating acute or chronic infection or inflammation.

Electrocardiogram (ECG)

A 12-lead ECG was taken at paper speed 50 mm/seconds when the patient was in the supine and resting positions. The resting heart rate was measured from the ECG data. All patients were at sinus rhythm at the time of admission.

The entire ECG data were scanned and transferred to a computer and the Adobe Photoshop software (Adobe Systems, Inc., San Jose, CA, USA) was used for 400% magnification. The QTc and Tp-e ECG measurements were carried out by 2 cardiologists who were blind to the patient data. Subjects who had a U wave in their ECG were excluded from the study. The QT interval was measured from the beginning of the QRS complex to the end of T wave. The heart rates were corrected using Bazett's formula [8,13]. The T wave was defined as the wave extending from the peak of T wave to the end of T. The Tp-e intervals were measured from precordial derivations. The Tp-e / QT ratio was calculated from these measurements.

Results

The clinical characteristics and laboratory parameters of the groups are presented in Table 1. Except for aspartate aminotransferase, total and low-density lipoprotein cholesterol and C-reactive protein levels, there was no statistically significant difference between the groups in terms of age, smoking, body mass index, or baseline laboratory values.

The ECG and echocardiography findings of the groups are given in Table 2.

The heart rate (76.4 ± 12.3 and 79.2 ± 13.6; p = 0.397), left ventricle ejection fraction (61.5 ± 2.4 vs. 61.4 ± 3.2; p = 0.557) left ventricle diastole end diameter (46.3 ± 3.1 vs. 47.5 ± 3.3; p = 0.467), left ventricle systole end diameter (28.0 ± 2.9'a vs. 29.7 ± 2.5; p = 0.299) and left atrium diameter (34.0 ± 2.9 and 33.6 ± 3.0; p = 0.382) were similar in both groups.

The QT interval (378.9 ± 41.4, 350.0 ± 22.7; p = 0.001), QTc interval (396.8 ± 46.7 and 367.3 ± 34.9; p = 0.039), Tp-e interval (68.2 ± 12.3 vs. 42.5 ± 6.8; p <0.001), Tp-e / QT ratio (0.18 ± 0.02 vs. 0.12 ± 0.01; p <0.001) and Tp-e / QTc ratio (0.17 ± 0.02 vs. 0.11 ± 0.01; p <0.001) were significantly higher in patients with preeclampsia than in controls.

Table 1. Demographic and laboratory data of the groups

Parameter	Patients (n=29)	Controls (n=30)	p value
Age (years)	33.4 ± 3.1	34.6 ± 2.6	0.29
Gravida	3 (2-4)	3 (1-4)	0.93
Parity	2 (1-3)	2(1-4)	0.88
Time over the index pregnancy (months)	24.4 ±7.7	21 ± 9.3	0.71
BMI (kg/m2)	27 (23±5.0)	26 (25.6±2.0)	0.81
Systolic BP (mmHg)	135 (110-155)	130 (100-150)	0.72
Diastolic BP (mmHg)	77 (60-95)	80 (65-90)	0.80
Glucose (mg/dl)	93±33	89±23	0.10
Hemoglobin (g/dl)	13.6± 1.6	14.0±1.0	0.39
Creatinine (mg/dl)	0.76±0.15	0.79±0.12	0.53
Total cholesterol (mg/dL)	175 ± 41	183 ± 38	0.77
LDL- cholesterol (mg/dL)	107 ± 41	105 ± 38	0.37
HDL- cholesterol (mg/dL)	43 ± 21	52± 20	0.83
Triglyceride (mg/dL)	175 ± 88	160 ± 63	0.83
AST (IU/L)	39 (14- 79)	35 (19- 45)	0.44
ALT (IU/L)	44 (13- 55)	22 (16- 44)	0.71
C-reactive protein (mg/L)	1.6 (0.9- 3.2)	1.2 (0.4- 5)	0.25

BMI: body mass index, BP: blood pressure, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine amino-transferase. Data are presented as mean±SD.

Table 2. Echocardiography and electrocardiography results of the groups

Parameter	Patients (n=29)	Controls (n=30)	p value
HR, beat/min	76.4±12.3	79.2±13.6	0.36
Tp-e, ms	68.2±12.3	42.5±6.8	<0.01
QT interval (ms)	378.9±41.4	350.0±22.7	0.001
QTc interval (ms)	396.8±46.7	367.3±34.	0.04
Tp-e / QT ratio	0.18±0.02	0.12±0.01	<0.001
Tp-e / QTc ratio	0.17±0.02	0.11±0.01	<0.001
LVEF, %	61.5±2.4	61.4±3.2	0.87
LVEDD (mm)	46.3±3.1	47.5±3.3	0.40
LVESD (mm)	LVESD, mm	29.7±2.5	0.22

HR-heart rate, LVEDD-left ventricular end-diastolic diameter, LVEF- left ventricular ejection fraction, LVESD-left ventricular end-systolic diameter, QTc-corrected QT, QTd-QT dispersion, Tp-e-T wave peak-to-end inter- val, Tp-ec- corrected Tp-e, Data are presented as mean±SD. .

Discussion

In this study, the QT interval, QTc interval, Tp-e interval, Tp-e/QT ratio and Tp-e/QTc ratio were found significantly higher in patients with a history of preeclampsia compared to the control group.

Despite extensive research, the exact etiopathogenesis of preeclampsia has not been fully explained so far (1). In the early weeks of gestation, the remodeling of spiral arteries becomes unsuccessful for reasons still not clear. As a result of this event, placental hypoperfusion and hypoxia occur. The generally accepted opinion is that the oxidative stress occurring due to antiangiogenic proteins and cytokines released from the hypoxic placenta triggers excessive systemic inflammatory response resulting in endothelial dysfunction and general vasoconstriction as well as end organ hypoperfusion [1-3].

In pregnancy, the balance between the proangiogenic factors (vascular endothelial growth factor [VEGF] and placental growth factor [PIGF]) and antiangiogenic factors (soluble Fms-like tyrosine kinase 1 [sFlt-1]) is critical. SFlt-1 binds to endothelial cell receptors and antagonizes VEGF and PIGF showing antiangiogenic effects [14]. Many studies have shown that sFlt-1 levels increase and PIGF and VEGF decrease in women with preeclampsia [14,15]. PIGF is present not only in placenta but also in the heart and lung tissues. Therefore, it is not surprising that changes in the sFIt-1 / PIGF ratio can involve cardiac or pulmonary effects [15].

Hypertension, proteinuria, exaggerated inflammatory environment, and insulin resistance have many common features with the preeclampsia metabolic syndrome characterized by endothelial dysfunction [6]. Preeclampsia has been associated with increased risk in the future years of the mother in terms of cerebrovascular diseases including arrhythmia, chronic hypertension, ischemic heart disease, type-2 diabetes mellitus, chronic kidney failure, and early death [2-6]. In the HAD MPS (Heart Failure and Arrhythmia after Maternal Placental Syndrome) study where more than a million women were reviewed retrospectively in Canada, placental syndrome (preeclampsia, placenta decollement and fetal prognosis) was found to develop in more than 75,000 mothers. It was shown that after the end of a 7-year period on the average, the prevalence of heart failure and arrhythmia increased in these women [4].

We have demonstrated in this study that there was an apparent change in the ventricular repolarization parameters in women whose pregnancy became complicated at least 12 months ago due to preeclampsia.

Conclusion

The most important step in the prevention of CVDs is the assessment and modification of risk factors [7]. In conclusion, although there is no guidance on the modification and screening of the cardiovascular risk factors in the female population with a history of preeclampsia or prospective randomized studies exploring the role of lifestyle changes in these patients, it is necessary to inform these women about the increased CVD risk in the advancing periods of their lives and to regulate the risk factors that can be modified (such as smoking and obesity).

Study limitations

The major limitations of this study are the relatively small sample size and cross-sectional design and lack of patient follow-up. The patients could not be prospectively followed up for arrhythmic episodes. Therefore, we could not precisely determine that an increased Tp-e interval and Tp-e/QT ratio predicts ventricular arrhythmias in patients with history of preeclampsia.

Competing interests
The authors declare that they have no competing interest.

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References

1. Steegers EA, von Dadelszen P, Duvekot JJ, et al. Pre-eclampsia. Lancet. 2010;376(9741):631-44.

2. Ray JG, Vermeulen MJ, Schull MJ, et al. Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. Lancet. 2005;366(9499):1797-803.

3. Adams T, Yeh C, Bennett-Kunzier N, et al. Long-term maternal morbidity and mortality associated with ischemic placental disease. Semin Perinatol. 2014;38(3):146-50.

4. Ray JG, Schull MJ, Kingdom JC, et al. Heart failure and dysrhythmias after maternal placental syndromes: HAD MPS Study. Heart. 2012;98(15):1136-41.

5. Ray JG, Booth GL, Alter DA, et al. Prognosis after maternal placental events and revascularization: PAMPER study. Am J Obstet Gynecol. 2016 Jan;214(1):106.e1-106.e14.

6. Garovic VD, Bailey KR, Boerwinkle E, et al. Hypertension in pregnancy as a risk factor for cardiovascular disease later in life. J Hypertens. 2010;28(4):826-33.

7. Mosca L, Benjamin EJ, Berra K, et al. Effectiveness-based guidelines for the prevention of cardiovascular disease in women-2011 update: a guideline from the american heart association. Circulation. 2011;123(11):1243-62.

8. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine Tenth Edition. Philadelphia: Elsevier; 2015;662-84.

9. Gupta P, Patel C, Patel H, et al. T(p-e) /QT ratio as an index of arrhythmogenesis J Electrocardiol. 2008;41(6):567-74.

10. Kirbas O, Biberoglu EH, Kirbas A, et al. Evaluation of ventricular repolarization in pregnant women with intrahepatic cholestasis. Int J Cardiol. 2015;189:25-9.

11. Açar B, Yüksel M, Yayla Ç, et al. Parameters of ventricular repolarization in patients with autoimmune hepatitis. Turk Kardiyol Dern Ars. 2017;45(4):333-8.

12. Demir M, Uyan U. Evaluation of Tp-e interval and Tp-e/QT ratio in patients with non-dipper hypertension. Clin Exp Hypertens. 2014;36(5):285-8.

13. Yaniel Castro-Torres, Raimundo Carmona-Puerta, Richard E Katholi. Ventricular repolarization markers for predicting malignant arrhythmias in clinical practice. World J Clin Cases. 2015;3(8):05–20.

14. Powe CE, Levine RJ, Karumanchi SA. Preeclampsia, a disease of the maternal endothelium: the role of antiangiogenic factors and implications for later cardiovascular disease. Circulation. 2011;123(24):2856-69.

15. Lecarpentier É, Vieillefosse S, Haddad B, et al. Placental growth factor (PlGF) and sFlt-1 during pregnancy: physiology, assay and interest in preeclampsia. Ann Biol Clin. 2016;74(3):259-67.