EVALUATION OF SURFACE ECG CHANGES IN PREGNANT WOMEN WITH GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Objective: Gestational diabetes mellitus (GDM) has an increased risk of maternal and fetal complications. Increased maternal cardiac risk is one of the most important complications. QT dispersion and Tp-e duration are findings of surface electrocardiogram (ECG) and they are used as an index of inhomogeneity in ventricular electrical activity, and prolongation of QT dispersion is related to increased incidence of ventricular arrhythmias. In this study, we aimed to investigate QT dispersion, Tp-e interval and Tp-e/QT ratio in pregnant women with GDM and emphasize the increased cardiac risk and the importance of GDM screening.

Methods: Thirty pregnant women with GDM (mean age 27.3±6.1 years) and 23 normal pregnant women (30.2±5.4 years) were included in the study. A 12-lead surface electrocardiogram was used to evaluate QT and Tp-e durations for all participants. All QT intervals were corrected for heart rate using *1*Ş L"2K, NBazett’s formula. QT dispersion was defined as the difference between the maximum corrected QT and minimum corrected QT duration. Student’s t test or Mann-Whitney U was used to compare groups. The results were evaluated at the p<0.05 significance level.

Results: Mean age, body mass index, blood pressure, heart rate and gestational week of pregnancy were similar between the two groups. QT dispersion (54±13 msc vs. 44±12 msc, p=0.006), Tp-e (81±7 msc vs. 76±8msc, p=0.013) and corrected Tp-e (102.4±9.7msc vs. 96.5±8.2msc, p=0.038) were significantly longer in pregnant women with GDM. The Tp-e/QT corrected ratio was found to be higher in GDM patients (0.19±0.01 vs. 0.18±0.02, p=0.040).

Conclusion: Our results suggest that QT dispersion, Tp-e interval and Tp-e/QTc ratio are increased in pregnant women with GDM compared to non-diabetic pregnant women. For this reason we suggest GDM screening for all healthy pregnant women and evaluation the long-term cardiac risks.

Key words: Gestational diabetes mellitus, QT dispersion, Tp-e interval, Tp-e/QT ratio.

Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy and which spontaneously recovers after delivery(1). The prevalence of GDM is about 2-6% of all pregnancies(2) and is the second most common endocrine disorder in pregnant women. However, the incidence of this endocrinopathy has increased in recent years due to an increase in obesity and age of expectant mothers(3). Pregnant women with GDM have an increased risk of maternal complications, including hypertension, preeclampsia, nephropathy and ketoacidosis. Furthermore, the risk of cardiovascular disease (CVD) is increased in the postpartum period of this population(4). It has also been established that there is an increase in inflammatory mediators, which create a risk of endothelial dysfunction and cardiovascular disease in pregnant women with gestational diabetes in subsequent years(5).

One of the methods used as an aid in diagnosing the increased risk in CVD cases is the QT dispersion (QTd), determined by surface electrocardiogram (ECG). (QTd) is an indicator of inhomogeneity in ventricular electrical activity(6). Prolonged QTd is correlated with an increased inci-
dence of ventricular arrhythmias and is a predictor of all causes of mortality\(^{(7,8)}\). QTd also increases in ischemic and hypertensive heart disease. Some studies have shown that QT and QTc intervals are longer in healthy women than in men\(^{(9)}\). Moreover, the average QTd is lower in the first trimester than in later periods of pregnancy and this prolonged QTd continues after delivery for 2 to 6 weeks\(^{(10)}\). The relation between insulin levels, metabolic syndrome, obesity and QT duration have been shown in some studies\(^{(11-14)}\). Recent studies have shown that the Tp-e interval, the terminal part of the QT interval described as the distance between the top of the T wave and the end of the T wave, is an index of total spatial dispersion of cardiac repolarization\(^{(15,16)}\). Prolongation of Tp-e has been associated with malignant arrhythmias in patients with CVD\(^{(17,18)}\).

There are limited studies on ECG changes during pregnancy. Nowadays there is still debate in GDM screening for healthy pregnant women, in this study we aimed to investigate whether there was a difference in QT dispersion, Tp-e interval and Tp-e/QT duration in women with gestational diabetes who have an increased risk of heart disease.

**Methods**

**Study population and laboratory analysis**

A total of 53 pregnant women, 30 with GDM and 23 without GDM, were enrolled in this observational and cross-sectional study in Çanakkale Onsekiz Mart University Medicine Faculty Hospital between April 2012- December 2. Gestational diabetes mellitus was defined, as two measurements of increased glucose in a 75 gr oral glucose tolerance test (OGTT) in 24-28\(^{th}\) gestational weeks of pregnancy routine screening. Fasting, 1 hour and 2 hour venous glucose levels were measured. The determined values were evaluated according to American Diabetes Association Criteria\(^{(19)}\). Fasting glucose level below 95, 1-hour glucose level below 180 and 2-hour glucose level below 155 were considered as normal values. All blood samples were obtained from venous blood and were studied with a Cobas e-601 (Roche Diagnostics, Indianapolis, USA) using a chemiluminescence method.

Patients who had all normal glucose levels were accepted as healthy controls. Patients with hypertension, electrolyte imbalance, chronic renal failure, chronic inflammatory disease, chronic lung disease, heart failure, valvular, structural or congenital heart disease, other endocrinologic disease, or smoking history were excluded. Glucose levels of all patients were back to normal within about one week after delivery. The study was approved by the Local Ethics Committee and written informed consent was obtained from all pregnant women.

In all cases, baseline variables of age, body mass index (BMI), gestational week, and blood pressure were recorded at the third trimester.

**Electrocardiography**

A 12-lead surface electrocardiogram (Nihon-KohdenCardiofax ECG1350K, Tokyo, Japan) was used to evaluate QT duration for all participants in their third trimester. The paper speed and amplitude were 50 mm/second and 20 mm/mV, respectively. QT duration was calculated as the time from the beginning of the Q wave up to the isoelectric TP segment for at least 3 cardiac cycles at each derivation. Maximum QT (QTmax) and minimum QT (QTmin) were recorded. Mean QT was calculated from all measured QT intervals. Tp-e interval was measured from the peak of the T wave to the end of the T wave for five consecutive beats and the arithmetic mean calculated\(^{(20)}\). All measurements were performed by one cardiologist who blinded to the clinical status of the pregnancy. All QT intervals were corrected for heart rate using Bazett’s formula (QTc interval=QT interval/square root of the RR interval)\(^{(21)}\). QTd was defined as the difference between QTcmax and QTcmin. Heart rate correction of Tp-e was calculated as has been done previously, similar to Bazzet’s formula: corrected Tp-e (cTp-e) = Tp-e/ square root of the RR interval\(^{(22)}\).

**Statistical Analysis**

Statistical analyses were performed using SPPS software (version 15.0, SPSS, Chicago, Illinois, USA). An assessment of the normality with Kolmogorov-Smirnov was done initially. All numerical data are expressed as mean±standard deviation or median (interquartile range). Mann-Whitney U or student t test was used to compare groups. The association between QTd and Tp-e interval with clinical features was evaluated with Spearman rank correlation analysis. A p value <0.05 was considered statistically significant.

**Results**

Mean age, BMI, gestational week, and blood pressure of pregnant women were similar between the two groups (Table 1). For all study groups, glu-
cose levels were well regulated by insulin or diet. Table 2 shows electrocardiographic results of the study population. Mean heart rate was found to be similar in pregnant women with and without GDM. QTd (54±13 msc vs. 44±12 msc, p=0.006) was prolonged in the GDM group. Tp-e (81±7 msc vs. 76±8 msc, p=0.013) and cTp-e (102.4±9.7 msc vs. 96.5±8.2 msc, p=0.038) were also significantly longer in pregnant women with GDM. Tp-e/QTc ratio was found to be higher in GDM patients (0.19±0.01 vs. 0.18±0.02, p=0.040).

A positive correlation was found between age and Tp-e, cTp-e and Tp-e/QTc ratio in correlation analysis (r=0.368, p=0.011; r=0.294 p=0.045 and r=0.293, p=0.046, respectively). In addition, a negative correlation was found between heart rate and Tp-e, Tp-e/QTc (r=-0.479, p<0.001 and r=-0.564, p<0.001 respectively) (Table 3).

Discussion

This study showed that ECG abnormalities may be associated with GDM. QTd, Tp-e, cTp-e, and Tp-e/QTc ratio were longer in pregnant women with GDM than in normal pregnant women. Each lead ECG indicated different repolarization durations derived from different myocardial areas. The difference between the longest and shortest QT interval is known as the QT dispersion. QTd is a noninvasive method that measures the homogeneity of ventricular electrical activity and prolonged QTd is correlated with an increased incidence of ventricular arrhythmias and myocardial ischemia, ventricular hypertrophy or dilatation, autonomic neuropathy, or electrolyte imbalance. It has been also suggested that QT and QTc intervals are longer in healthy women than in men.

Dysrhythmias most commonly occur during pregnancy in women with cardiac abnormalities, but also in women with structurally normal hearts. Although the frequency of life-threatening dysrhythmias is unclear, hormonal and hemodynamic changes can cause an increased tendency to dysrhythmia. Lechmanova et al reported that the average QTd is longer in later periods than in early peri-

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Heart Rate (bpm)</th>
<th>QTmax (msc)</th>
<th>QTmin (msc)</th>
<th>QTmean (msc)</th>
<th>QTd (msc)</th>
<th>Tp-e (msc)</th>
<th>Tp-e corrected</th>
<th>Tp-e/QT</th>
<th>Tp-e/QTc</th>
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<tbody>
<tr>
<td>Pregnants without GDM (n=23)</td>
<td>27.3±5.4</td>
<td>310±29</td>
<td>326±28</td>
<td>441±23</td>
<td>396±23</td>
<td>418±22</td>
<td>96.5±8.2</td>
<td>0.23±0.02</td>
<td>0.18±0.02</td>
</tr>
<tr>
<td>Pregnants with GDM (n=30)</td>
<td>30.2±9.4</td>
<td>315±23</td>
<td>335±23</td>
<td>448±26</td>
<td>393±21</td>
<td>418±20</td>
<td>102.4±9.7</td>
<td>0.24±0.02</td>
<td>0.19±0.01</td>
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<tr>
<td>p</td>
<td>0.097</td>
<td>0.575</td>
<td>0.231</td>
<td>0.304</td>
<td>0.630</td>
<td>0.987</td>
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<table>
<thead>
<tr>
<th>QTd</th>
<th>Tp-e</th>
<th>cTp-e</th>
<th>Tp-e/QT</th>
<th>Tp-e/QTc</th>
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<tr>
<td>0.160</td>
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<td>-0.245</td>
<td>-0.070</td>
<td>-0.564</td>
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<tr>
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<td>&lt;0.001</td>
<td>0.077</td>
<td>0.618</td>
<td>&lt;0.001</td>
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Table 3: Correlation analysis of relations between QTd, Tp-e durations and clinical risk factors.
ods of pregnancy\textsuperscript{(20)}. Ozmen et al could not find a difference in QTd between pregnant and non-pregnant women. But since they did not separate trimesters for the study groups, this may be the reason for a lack of difference\textsuperscript{(27)}.

Medova et al showed that in pregnant women the QTd was longer than for control subjects and in pregnant women with GDM it was longer than for normal pregnancies and for control subjects\textsuperscript{(28)}. Our results suggest that QTd was longer in pregnant women with GDM. Isik et al reported that fasting blood glucose was an independent predictor of QTc and QTd in patients with metabolic syndrome\textsuperscript{(29)}. Newbern et al suggested that increased production of placental prolactin in GDM can cause activation of sympathoadrenergic activity and an increase of intraventricular electrical conduction\textsuperscript{(30)}. This hormonal and metabolic difference in patients with GDM may explain the electrocardiographic difference.

Tp-e interval and Tp-e/QT ratio can be used as an index of total ventricular repolarization, as indicated in recent studies\textsuperscript{(31-34)}. Ericksson et al reported that long Tp-e has been associated with malignant arrhythmias and mortality in patients with myocardial infarction. They also found a strong association between long Tp-e and non-fatal arrhythmia and Tp-e, which correlated with age, heart failure, ejection fraction, heart rate, and QT duration\textsuperscript{(34)}. The Tp-e/QT ratio may possibly be a more accurate marker of ventricular heterogeneity of repolarization than the QTd and Tp-e interval\textsuperscript{(30)}. In this study, we found that Tp-e, cTp-e and Tp-e/QTc ratio were longer in pregnant women with GDM than in non-diabetic pregnant women. Tp-e and Tp-e/QT ratio were positively correlated with age.

Small population size is the major limitation of our study. Patients could not be followed up prospectively, especially in postpartum, in terms of long-term cardiac arrhythmia detection.

**Conclusion**

Our results indicate that increased ventricular repolarization heterogeneity could be related to an increased prevalence of ventricular arrhythmias and cardiovascular mortality in GDM patients. Moreover, this result shows diabetes mellitus screening is important in terms of prevention and counselling for heart disease that may develop in the future for pregnant women without any health problem. These pregnant women with GDM must be informed in terms of the long-term increased risks.

**References**

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Evaluation of surface ECG changes in pregnant women with gestational diabetes mellitus

Gestational Diabetes Mellitus.


"duration of P: does this have clinical significance?"


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